A STUDY TO ESTIMATE THE PREVALANCE OF THYROID DYSFUNCTION AND TO ASSESS THE CORRELATION BETWEEN THYROID HORMONE LEVELS AND THE SEVERITY OF PSYCHOPATHOLOGY IN PATIENTS WITH SCHIZOPHRENIA

DISSERTATION SUBMITTED FOR PARTIAL FULFILLMENT OF THE RULES AND REGULATIONS

DOCTOR OF MEDICINE

BRANCH XVIII (PSYCHIATRY)

THE TAMIL NADU DR. MGR MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU

APRIL 2016

CERTIFICATE

This is to certify that the dissertation titled "**A STUDY TO ESTIMATE THE PREVALANCE OF THYROID DYSFUNCTION AND TO ASSESS THE CORRELATION BETWEEN THYROID HORMONE LEVELS AND SEVERITY OF PSYCHOPATHOLOGY IN PATIENTS WITH SCHIZOPHRENIA"** is the bonafide work of **Dr. PARVATHY J RAVIKUMAR,** in part fulfillment of the requirements for the MD Branch – XVIII (Psychiatry) examination of The Tamilnadu Dr. M.G.R Medical University, to be held in April 2016. The period of study was from June 2015- August 2015.

The Director,
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CERTIFICATE OF GUIDE

This is to certify that the dissertation titled **"A STUDY TO ESTIMATE THE PREVALANCE OF THYROID DYSFUNCTION AND TO ASSESS THE CORRELATION BETWEEN THYROID HORMONE LEVELS AND SEVERITY OF PSYCHOPATHOLOGY IN PATIENTS WITH SCHIZOPHRENIA"** is the original work of **Dr. PARVATHY J RAVIKUMAR,** done under my guidance submitted in partial fulfillment of the requirements for the MD Branch – XVIII (Psychiatry) examination of The Tamilnadu Dr. M.G.R Medical University, to be held in April 2016.

Dr. P.P.KANNAN, MD, DPM
Associate Professor,
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DECLARATION

I, **Dr. PARVATHY J RAVIKUMAR,** solemnly declare that the dissertation titled, "**A STUDY TO ESTIMATE THE PREVALANCE OF THYROID DYSFUNCTION AND TO ASSESS THE CORRELATION BETWEEN THYROID HORMONE LEVELS AND SEVERITY OF PSYCHOPATHOLOGY IN PATIENTS WITH SCHIZOPHRENIA",** is a bonafide work done by me at the Madras Medical College, Chennai, during the period from June 2015-August 2015 under the guidance and supervision of **Dr. P.P.KANNAN, MD, DPM,** Associate Professor of Psychiatry, Madras Medical College.

The Dissertation is submitted to The Tamilnadu Dr.M.G.R.Medical University towards part fulfillment for MD Branch XVIII (Psychiatry) examination.

Place:

Date: **Dr. PARVATHY J RAVIKUMAR**

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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CERTIFICATE OF APPROVAL

To
Dr.Parvathy J Ravikumar
Post Graduate M.D.(Psychiatry)
Madras Medical College
Chennai 600 003

Dear Dr.Parvathy J Ravikumar,

The Institutional Ethics Committee has considered your request and approved your study titled **"A study to estimate the prevalence of Thyroid dysfunction and to assess the correlation between thyroid hormone levels and severity of psychopathology in patients with schizophrenia" No.18052015.**

The following members of Ethics Committee were present in the meeting held on 12.05.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
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10. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

12/6/15

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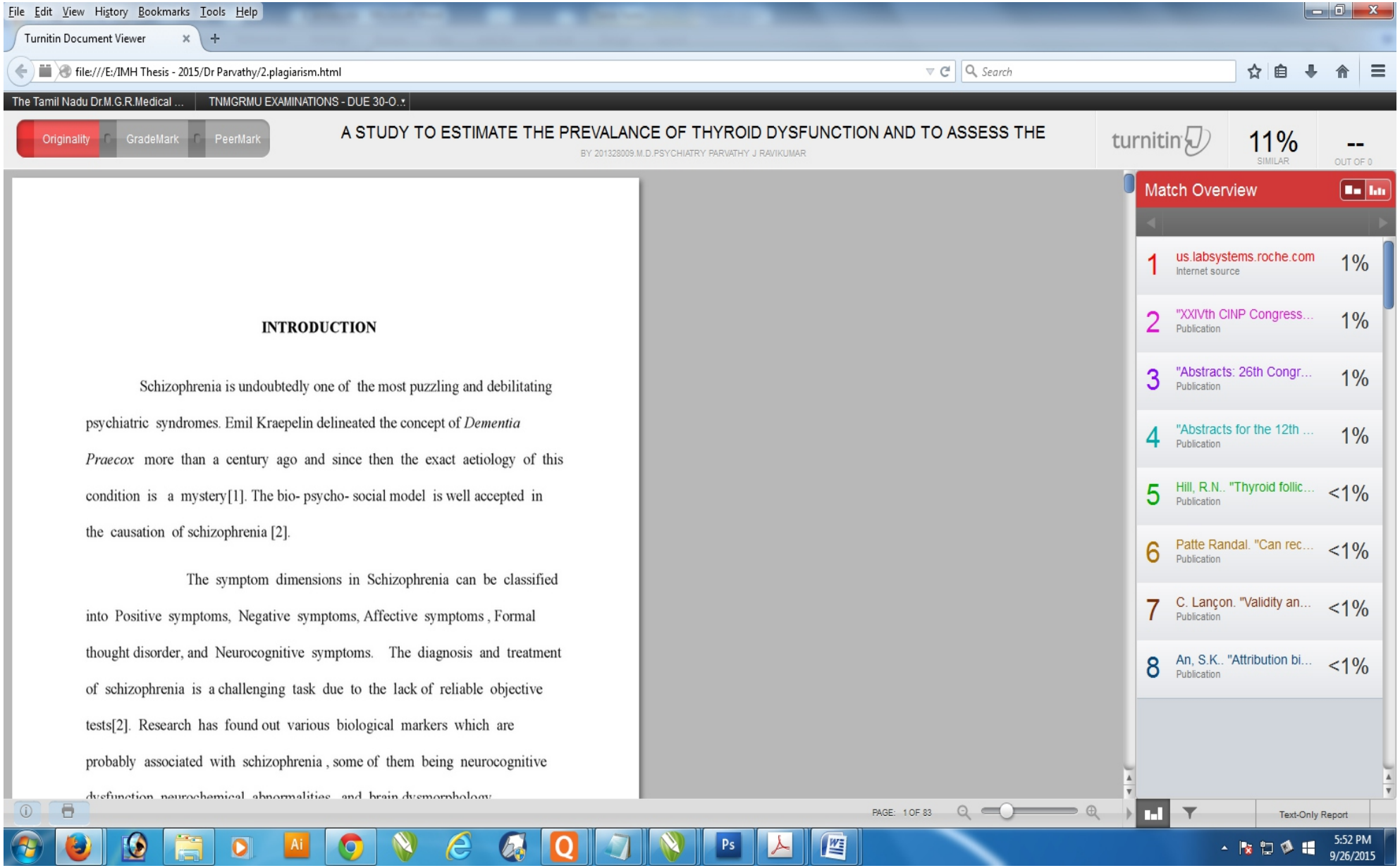
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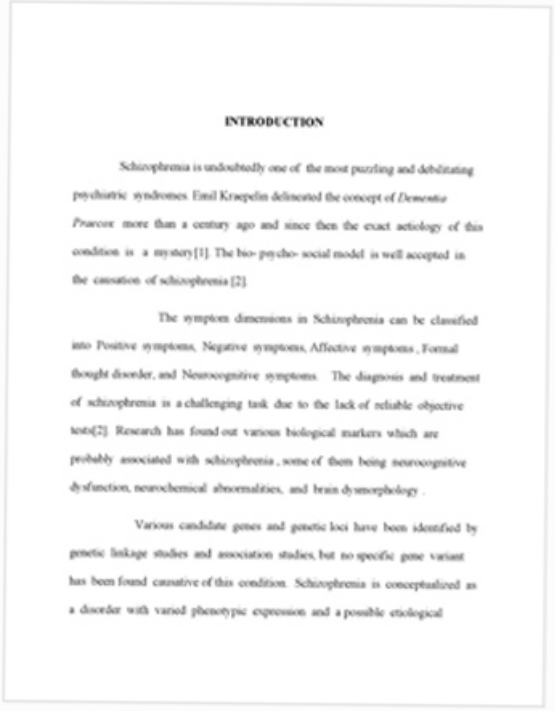

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Various candidate genes and genetic loci have been identified by genetic linkage studies and association studies, but no specific gene variant has been found causative of this condition. Schizophrenia is conceptualized as a disorder with varied phenotypic expression and a possible etiological

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Various candidate genes and genetic loci have been identified by genetic linkage studies and association studies, but no specific gene variant has been found causative of this condition. Schizophrenia is conceptualized as a disorder with varied phenotypic expression and a possible etiological contribution from the interaction between genetic susceptibility and environmental influences[1].

Thyroid hormones play a major role in regulating almost all the organ systems in our human body. It has a modulating role in the metabolic rate of the body, temperature regulation, and the normal functioning of cardiovascular system, central nervous system and the skeletal system.

The relationship between the human brain and thyroid gland is bidirectional. The Hypothalamic- Pituitary- Thyroid axis is regulated by various central pathways. The thyroid hormones in turn affect the cognitive and affective functions of the brain.

It has been postulated that hormones and vitamins can serve as modulators of gene environment interactions in schizophrenia[4]. The existing evidence favors the role of thyroid hormones to act as bridges in the pathway between candidate genes, environmental influences and the ultimate phenotypic expression of the disorder. Thyroid hormones have a significant role in influencing the normal functioning of neurotransmitter pathways and in the normal development and regulation of the central nervous system. The available data to the best of current knowledge supports the thyroid hormone hypothesis in Schizophrenia[4].

The abnormalities in thyroid hormones can produce various psychiatric manifestations like mood disorders, cognitive , anxiety, and psychotic disorders[5]. Considering the critical role of thyroid hormones

in psychiatry, it is a routine practice in most of the mental health centres to screen for thyroid dysfunction in their inpatients. The relevance of thyroid hormones in bipolar disorder is well established. The two conditions namely Bipolar Disorder and Schizophrenia have a significantly high degree of genetic transmissibility. Various candidate genetic markers of both the conditions are located on the same chromosomes. Recent research has notably raised the question of bipolar disorder and schizophrenia lying along a continuum[6].

There has been case reports of psychotic presentations of hypothyroidism as well as hyperthyroidism[7]. Asher has described the typical clinical manifestations of psychosis induced by hypothyroidism in 1949[8]. Research has identified that thyroid hormone abnormalities can cause acute psychotic presentations also[9]. Despite all of the above facts, there has not been much data on the association between thyroid hormones and Schizophrenia. Indian studies on the prevalence of thyroid abnormalities in psychiatric disorders are also lacking[10].

The existing data has shown that the rates of thyroid hormone abnormalities in schizophrenia are comparable to that in mood disorders[10]. Most of the studies have focused on the levels of Thyroid Stimulating Hormone and the variations in the levels of Thyroid hormones during the course of the illness and with neuroleptic treatment.

The course of schizophrenia in the Indian population as reported by Thara et al showed that 36% of the subjects had multiple relapses with incomplete remission. However, 80% of the study population who had stopped taking their medication were in different stages of remission. Considering this fact, it can be told that the data on the role of thyroid homones in influencing the progress of the schizophrenic illness is deficient. There is only limited literature in the Indian Population on the prevalence of thyroid hormone abnormalities in schizophrenic patients.

SCOPE OF THE STUDY:

Even though much data has been published in the Western literature regarding the state of thyroid hormones in mood disorders, literature is lacking in schizophrenia. The existing data has yielded conflicting results. Indian studies are also lacking in this field. The purpose of this study is to bridge the gap in this area. The current study tries to evaluate the thyroid hormone abnormalities in patients diagnosed with Schizophrenia in the Indian context and also seeks whether any association with psychopathology exists.

REVIEW OF LITERATURE

The review of literature will be dealt with under three headings.

a. The physiology and laboratory measurements of thyroid hormones
b. The neuropsychological aspects of thyroid diseases
c. The existing data on the relevance of thyroid hormones in schizophrenia.

I.THE PHYSIOLOGY OF THYROID HORMONES

THYROID GLAND:

The thyroid gland is located in the front of neck, inferior to the larynx and cricoid cartilage. The gland has two lobes, each lobe being 5cm in length, which are joined together by a narrow band of thyroid tissue called isthmus. The lobes lie on either sides of the oesophagus and trachea. The thyroid gland is covered by a fibrous capsule which extends into the body of the gland creating septae. These septae divide the gland into lobules.

The gland is normally palpable in 50% of the women and almost 25% of men. The thyroid consists of approximately one million spherical follicles, also known by the name acini. These follicles are made up of a layer of cuboidal epithelium and is filled with a proteinacious material called colloid. The size of the follicular cells depends on the activity level

of the thyroid gland. The lining cuboidal epithelial cells are flat and follicles are filled with colloid if the gland is “inactive” whereas the “active” thyroid gland is made of small follicles, scanty colloid , and the epithelial cells are tall , columnar with scalloped edges forming reabsorption lacunae.

The colloid in the follicle contains iodinated Thyroglobulin. Between the follicles there are another group of cells known as the “parafollicular cells”, also called as the “C cells”. The function of the follicular cells is to produce the thyroid hormones T3, T4 and reverse T3 (rT3) and secrete them into the blood circulation whereas that of the parafollicular cells is to synthesise another hormone Calcitonin.

The follicular cells also serve the function of iodine uptake from the circulating blood in the capillaries, into the colloid inside the follicle and synthesis of Thyroglobulin.

THE SYNTHESIS, STORAGE AND RELEASE OF THYROID HORMONES:

The thyroid gland needs an adequate supply of iodide from the blood stream for the synthesis of thyroid hormones. Thyroid gland is a unique endocrine gland in that it is the only tissue in our human body which is capable of storing iodine in large quantities and utilizes it by

incorporating into the hormones it secretes. The steps involved in the production of thyroid hormones are much complex and consists of a sequence of events as follows.

A. ACTIVE UPTAKE OF IODIDE BY THE FOLLICULAR CELLS

The first step in the production of thyroid hormones is the active uptake of iodide in the blood by the thyroid gland. This takes place with the help of iodide pump, which is an active transport mechanism. This step is regulated by the Thyroid Stimulating Hormone (TSH) secreted by the Anterior Pituitary gland. An average dietary intake of 150mcg of iodine is required for the synthesis of thyroid hormones.

B. OXIDATION OF IODIDE AND FORMATION OF IODOTYROSINES

The second step is the oxidation of iodide into active iodine, which is used for iodinating the tyrosyl residues of thyroglobulin. This reaction is catalysed by the enzyme Thyroid Peroxidase (TPO) in the presence of Hydrogen peroxide and iodide. The reaction takes place in the apical border of the cells and ultimately results in the formation of Diiodotyrosine (DIT) and a relatively small share of Monoiodotyrosine (MIT).

B. COUPLING OF IODOTYROSINE RESIDUES

There occurs coupling of two DIT molecules or one DIT molecule with one MIT molecule to form the peptide hormones, T4 and T3. Some of the DIT molecules also combine with MIT molecule to produce reverse T3. These reactions are also takes place in the presence of the Peroxidase enzyme.

C. PROTEOLYSIS OF THYROGLOBULIN AND RELEASE OF IODOTHYRONINES

Endocytosis of colloid droplets into the follicular epithelial cells happens and proteolysis occurs thereby releasing the compounds MIT, DIT, T3, and T4. The formed MIT and DIT are recycled into the colloid to continue the process and the synthesized thyroid hormones are secreted into the circulation. The thyroid gland secretes 4mcg T3 and 80mcg T4 each day.

THE TRANSPORT, METABOLISM AND EXCRETION OF THYROID HORMONES

A. CONVERSION OF THYROXINE TO TRIIODOTHYRONINE

The thyroid gland secretes T4 almost 8 to 10 times the rate of T3. The thyroid hormone T4 is considered as a prohormone and since it has a longer half life, the concentration in blood is always much higher than T3.

The secreted T4 undergoes 5’ deiodination to yield T3 and another deiodination reaction in the inner ring to give reverse T3 (rT3), which is an inactive compound. About 33% of secreted T4 is converted to T3 and another 40% to rT3.

B. TRANSPORT OF THYROID HORMONES IN BLOOD

The thyroid hormones circulate in the plasma in bound form through non covalent association with the plasma proteins Thyroxine binding Pre Albumin (TBPA), Thyroxine Binding Globulin (TBG), and albumin. Only 0.02% of T4 and 0.3% of T3 are in the free and unbound form in the circulation which takes part in the physiological actions of the hormones.

C. METABOLISM AND EXCRETION

Deiodination is the major metabolic pathway of thyroid hormones in humans and approximately 87% of T3 in the circulation is formed by this process from T4. Degradation occurs in the liver and hormones get converted by conjugation into sulfate or glucuronide and is excreted into the intestine via bile. A small portion is hydrolysed by the intestinal bacteria and rest undergoes enterohepatic circulation and is excreted in feces in the unconjugated form.

REGULATION OF THYROID HORMONE SECRETION

The anterior pituitary secretes Thyroid –Stimulating Hormone (TSH) which increases the activities of the Thyroid Gland and stimulates

it to secrete its hormones. TSH inturn is regulated by a peptide hormone Thyrotropin Releasing Hormone (TRH) secreted by the Hypothalamus into the Hypothalamic portal system. The equilibrium is maintained by a negative feedback system exerted on TSH and TRH by the thyroid hormones.

PHYSIOLOGICAL ACTIONS OF THYROID HORMONES

The thyroid hormones enter the cells by a process of diffusion or specific transport and binds to the nuclear receptors – hTR- α 1 and hTR- β 1and exerts action on various body tissues.

a. CARDIOVASCULAR SYSTEM:

Thyroid hormones increase the affinity and number of beta adrenergic receptors, known as the chronotropic effect and also increase the response to circulating catecholamines, known as the inotropic effect

b. ADIPOSE TISSUE:

The overall effect is catabolic by stimulating lipolysis.

c. MUSCLE:

Increases protein breakdown and has a catabolic effect

d. BONE: Has a metabolic and developmental effect by promoting normal growth and skeletal development and also accelerates born turn over.

e. **NERVOUS SYSTEM:** promotes normal brain development. Hyperthyroid individuals exhibit features of anxiety, hyperreflexia, and tremors. Persons with myxoedematous illness have behavioural disturbances and sluggishness.

f. GUT: increases rate of carbohydrate absorption.

g. LIPOPROTEIN: stimulates formation of LDL receptors

h. OTHER EFFECTS: increases metabolic rate and stimulates Oxygen consumption thereby exerting a calorigenic effect.

DISORDERS OF THYROID FUNCTION AND LABORATORY ASSESSMENT

Thyroid dysfunction can be assessed by doing the available thyroid function tests.

1. TSH TEST:

On measuring, if the TSH levels are high, this means that the thyroid gland is functioning inadequately due to pathology primarily affecting the gland itself (primary hypothyroidism).

If the TSH levels on measuring are low, it means that the thyroid gland is hyperactive and producing excess of hormones and the condition is hyperthyroidism.

If there is any pathology in the pituitary gland, TSH levels will be low. In such conditions, sufficient TSH will not be available to stimulate the thyroid gland, resulting in secondary hypothyroidism.

In healthy individuals , a normal TSH value obtained means that the thyroid gland is functioning normally.

Normal TSH level is 0.3-4.7mIu/ml.

2. T4 (THYROXINE TEST):

The most important test to assess thyroid function is the free T4 fraction and tests used is Free T4 (FT4) and the Free thyroxine index (FT4 index).In hyperthyroidism, there is a low TSH level and a high T4 level. A low TSH with low FT4 or FTI is due to hypothyroidism arising out of pathology in the pituitary gland. A high TSH level with a low FT4 or FTI value suggests primary hypothyroidism due to pathology in the thyroid gland itself.

Normal values of

a. serum thyroxine : 4.6 -12 $\mu g/dl$

b. free thyroxine FT4: 0.7-1.9 $\mu g/dl$

c. free thyroxine index FTI : 4.6 – 12

3. TRIIODOTHYRONINE (T3) TEST :

T3 testing is mainly used for the diagnosis of hyperthyroidism and has less diagnostic value in detecting hypothyroidism. This test is also used to assess the severity of hyperthyroidism.

In hyperthyroidism, there is high levels of T3 and low levels of TSH. In hypothyroidism ,there is low levels of T3 and high TSH values.

T3 values are the last to get deranged in cases of hypothyroidism.

NORMAL VALUES OF

a. serum triiodothyronine (T3): 80 -180 ng/dl

b. Free T3 index FT3I: 80 -180.

INTERPRETATION OF RESULTS

T3	T4	TSH	INTERPRETATION
Normal	Normal	High	Subclinical Hypothyroidism
High or normal	High or normal	Low	Hyperthyroidism
Low or normal	Low	High	Hypothyroidism
Low or normal	Low or normal	Low	Pituitary (secondary hypothyroidism)

II. NEUROPSYCHIATRIC MANIFESTATIONS OF THYROID DISORDER

The overlap between the functions of the thyroid gland and the neuropsychiatric functions is a very delicate and intriguing one. Patients presenting with neuropsychiatric manifestations produced by thyroid dysfunction, respond well when the derangement in thyroid function is corrected , eventhough some patients may continue to exhibit symptoms in varying severity. Characteristic symptoms are triggered by thyrotoxicosis whereas the manifestations of hypothyroidism are much

non specific. The probable explanation as to why thyroid disorders should cause psychiatric manifestations have been hypothesized to be its effect on neurotarnsmitters, and other hormonal activation[11].

PREVALANCE OF THYROID DYSFUNCTION

It is difficult to analyse the wide spectrum of studies available on the epidemiological data on thyroid disorders. This could be attributed due to the differences in the study populations selected with respect to age, geographical distribution and sample size.

HYPOTHYROIDISM:

In the general population, it is estimated that hypothyroidism exists in the range between 0.5 to 18% of the total population. Desai PM et al conducted an Indian study in 1997 and found out that 42 million of the population suffer from thyroid disorders in the Indian subcontinent [12]. In a study conducted in Kerala, the prevalence of subclinical hypothyroidism was found out to be 9.4% and that of hypothyroidism to be 3.9% [13].

The Whickham survey carried out in the Northern England concluded that there exists a gender variation in the prevalence of thyroid dysfunction[14]. The study found out a mean incidence of 4.1/ 1000 per year of hypothyroidism in women and 0.6/1000 per year in men[15].

HYPERTHYROIDISM IN GENERAL POPULATION

The data from Kerala reported that the prevalence of overt hyperthyroidism was 1.3% and subclinical hyperthyroidism was 1.6%[13]. The Whickham survey found out a mean incidence of 0.8/1000 per year of hyperthyroidism in women and there was no significant incidence rates in men[14]. A hospital based study conducted in Pondichery reported the prevalence of subclinical and overt hyperthyroidism to be 0.6% and 1.2% respectively[16].

THYROID AND PSYCHIATRY

Jain and Gautam et al conducted a hospital based study and found out the prevalence of total psychiatric comorbidity in thyroid dysfunction to be 58.33%[17]. Depressive disorder was more than anxiety disorder in prevalence in patients with thyroid disorder (11.8% when compared to 5.4%). In hypothyroid individuals, the prevalence of depression was 33% and that of anxiety disorder was 20%.

In hyperthyroid individuals, depression was found in 55% and anxiety in 60% of the sample, which meant the rates differed significantly only in hypothyroidism. The prevalence of various subtypes of anxiety disorder were panic disorder (5.0-45.6%), social phobia (7.4-8.7%), Obsessive Compulsive Disorder(7.4%) and Generalised Anxiety Disorder

(41.2%)[18]. Women carry a ten fold higher risk of hypothyroidism than men.

Both hyperthyroidism and hypothyroidism cause changes in mood and intellectual performance. Severe hypothyroidism can mimic melancholic depression and dementia. Hypothyroidism can present mainly with psychiatric manifestations which can often mislead the treating physician. A high degree of suspicion should be executed in evaluating patients presenting with predominantly affective, cognitive and behavioural disturbances.

THYROID AND PSYCHOSIS

It was Von Basedow who initially described a psychotic presentation, probably mania, in a patient with exophthalmic goiter. Case reports are being reported of psychotic manifestations with depressive, manic and schizophreniform features.

Hashimoto encephalopathy is a rare clinical presentation presenting with psychotic features ,which is related to Hashimoto's thyroiditis. The psychoses occurs probably because of the development of autoimmune vasculitis , together with cerebral oedema. It can also result from the harmful effects of Thyrotropin Releasing Hormone (TRH). Perceptual changes can occur in any sensory modality. There may be changes in

vision , hearing and taste. As the disease progresses, the delusions and hallucinations also increase in severity.

Asher described Myxoedema Madness and it continues as one of the most cited references even today. The manifestations of psychoses due to hypothyroidism vary and there are no specific cluster of symptoms by which patients seek treatment. An individual case report of Capgras syndrome has also been reported in myxoedema. Psychosis characteristically surfaces years after the development of myxoedema. Delusions, hallucinations, loosening of associations and paranoia are frequently reported, secondary to myxoedema.

A case report of Periodic catatonia ,and Delusional Misidentification syndrome which includes both Capgras and Fregoli syndrome occuring in the same individual with subclinical hypothyroidism has been reported[19]. The laboratory values revealed an elevated TSH ,along with normal T3 and T4. Levothyroxine supplementation and reinstating the euthyroid state resolved the symptoms. This was the only case report of delusional misidentification responding to levothyroxine[19].

Psychosis can also occur secondary to hyperthyroidism, eventhough it’s a rarity (1% of the cases). Most of the patients would have received a prior diagnosis of mania or delirium before coming to

know about their thyroid status. Psychosis in the context of hyperthyroidism , are mostly affective psychosis[20]. Case reports of individuals presenting with depression and psychosis have been published[20]

Increased circulating thyroid hormones in the body, as seen in thyrotoxic crisis, can induce psychotic features in the form of persecutory delusions and paranoid behavior [21]. Acute psychosis like presentations are also seen in severe thyrotoxic crisis[22].

The severity of psychotic symptoms are unrelated to the degree of thyroid hormone deficiency. In some cases,symptoms remit on thyroid hormone supplementation and in some others, symptoms are irreversible.

THYROID AND AFFECTIVE DISORDERS

Thyroid hormone treatment was found to be efficacious in cases of refractory depression and in refractory bipolar depression. It was hypothesized that poor response to treatment modalities in bipolar depression could be attributed to subnormal levels of circulating thyroid hormone levels. Thomas J Stamm, MD et al tested the above hypothesis and reported that women respond better when adjunctive treatment with supraphysiologic doses of levothyroxine was added to treatment regimen in resistant cases of bipolar depression[23]. The study failed to show a

statistically significant outcome when it was compared to the group treated with placebo.

The TSH response may be blunted or exaggerated in response to subliminal doses of TRH in cases of depression. Since long, the blunted response of TSH is made use of as a marker for endogenous depression. The possible explanation for the association between thyroid hormones and mood disorders could be linked to its action on the neurotransmitter systems involved in mood regulation. The action of thyroid hormones in serotonin system is by decreasing the sensitivity of 5-HTIA autoreceptors found in the raphe area and by increasing the 5-HT2 receptor sensitivity with a net effect of increasing the serotonergic transmission[24]. It has also been found out that brain serotonin results correlate positively with serum T3 levels, which means that serotonin synthesis is decreased in hypothyroidism.

Clinical and subclinical hypothyroidism can affect the course of bipolar disorder negatively. Studies have also shown that low normal values of free T4 index and higher normal values of TSH were significantly associated with delay in response to treatment and less favorable outcome.

In the initial phase of hyperthyroidism, there is adrenergic stimulation effected by the increased thyroid hormones, which can induce

mania[25]. Case reports of Graves disease with mania are available. As time passes, there will be adrenergic exhaustion caused by excessive stimulation and ultimately results in depression[25]. Thyroid hormones also have a modulating effect in dopamine post- receptor and signal transducing processes, and also post synaptic beta adrenergic activity[26].

THYROID AND ANXIETY DISORDERS

The beta adrenergic overactivity induced by hyperthyroidism can result in anxiety symptoms. One of the medical causes identified for anxiety disorder is hyperthyroidism[27]. A pleiotropic syndrome characterized by mitral valve prolapse, thyroid disorders, panic disorder, severe headaches and urinary bladder problems was identified recently[28]. Studies have shown that this syndrome could be associated with specific genes mapped on chromosome 13q as well as on chromosome 22[28].

The association between anxiety disorders and thyroid hormones could not be replicated in some of the studies. An etiological relationship between generalized anxiety disorder and thyroid disorder could not be found out because of the absence of any mild abnormalities in thyroid hormonal status in this population.

THYROID AND COGNITIVE DISORDERS

Cognitive impairment can arise from both hypothyroidism and hyperthyroidism. Both higher and lower TSH values, even though lying in the normal range, are found to be associated with poor cognition[29]. Thyroid hormones negatively regulate the expression of the amyloid-β protein precursor, which plays a major role in the pathogenesis of Alzheimer's Dementia. A decrease in the levels of Thyrotropin Releasing Hormone (TRH) can increase the phosphorylation of tau protein which is implicated in the etiopathogenesis of Alzheimer's disease.

Neurocognitive deficits that occur in thyroid dysfunction affect areas of general intelligence, psychomotor speed, working memory and long term memory and visuo-spatial speed. Retrieval deficits are seen in thyroid disorder rather than deficits in encoding or attention. Elderly individuals are more likely to suffer from cognitive deficits due to hypothyroidism.

THYROID AND SCHIZOPHRENIA

The association between thyroid hormones and psychotic disorders have been studied as early as in 1888 by a committee of the clinical society in London[30]. Research has been done extensively about the modulating role of thyroid hormones in affective illness and its role in the

pathophysiology of Mood disorders[31,32]. The dopaminergic, serotonergic, GABA ergic and glutamatergic neurotransmitter networks are influenced by thyroid hormones[33-36]. The misregulation in these networks are well implicated in Schizophrenia also. Hence the relevance of thyroid hormones in Schizophrenia cannot be overemphasized.

The heterogeneity and complexity of Schizophrenia makes it difficult to demarcate the etiological interactions between the genetic and environmental factors. It is postulated that the environmental insults occur from the perinatal period itself [37]. A clear understanding about the molecular mechanisms in schizophrenia is lacking and till date no specific biomarker has been identified.

In this context, the regulation by the multiple receptors of transcriptional activity can be considered as potent factors in sealing the gap between environmental contributors and genetic factors in schizophrenia. Thyroid hormones are one among these.

Several groups of researchers have measured the thyroid hormone levels and other parameters in relation to thyroid gland in patients of schizophrenia. Both hospitalized patients and outpatients have been included in such studies and derangements reported. Prior to the mid 1980s, sensitive assays for measuring thyroid hormones, especially the

free hormones were not available. Now the availability of highly sensitive and specific methods makes it easier to assess the free thyroid hormones.

To date, almost 15 studies have independently analysed the thyroid hormone values in schizophrenia patients. Rinieris et al conducted a study on drug free(for atleast 3 weeks) schizophrenia patients and measured their FreeT4 and Total T4 values in serum before and after neuroleptic treatment. The study reported a decrease in both the total and free T4 fraction after pharmacotherapy with Chlorpromazine and Clozapine[38]. The study concluded with a note that serum thyroid hormone levels need to be analysed before and after antipsychotic treatment[38].

To assess the relationship between neurotransmitters and thyroid hormones in schizophrenia, Rao et al measured the serum levels of thyroid ormones and neurotransmitters involved in ten acutely ill schizophrenia patients and in ten healthy subjects. They found out that the levels of dopamine was increased and that of thyroid hormones was decreased in schizophrenia patients. The authors concluded that increased dopamine activity in schizophrenia affected the function of the pituitary gland and decreased the secretion of TSH[39].

Effect of treatment on thyroid status was also evaluated by Martinos A et al,where they assessed the function of pituitary thyroid axis after six weeks of neuroleptic treatment and the response of TSH to

thyrotropin releasing hormone with respect to its diurnal variation. TRH stimulation test was performed in each of the twenty five male schizophrenia patients selected for the study at 14.00 h and 24.00 h of the same day, both before and after treatment with antipsychotics. Increased TSH values at the baseline and an exaggerated TSH response to TRH was obtained in the post treatment phase. The study made an assumption that subclinical hypothyroidism may exist in patients with schizophrenia who are on treatment regimen with antipsychotics.

Mason et al analysed the thyroid hormonal levels longitudinally at admission and every two weeks after that. An average of four samples per patient was collected. The study reported that free T4 values increased through the course of the study in paranoid schizophrenia subgroup, even when lying in the normal range[41]. There is a need for assessing thyroid function longitudinally in the course of schizophrenia and the initial analysis has to be interpreted with caution.

A study by Southwick et al also concluded that there exists a change in the serum levels of T4 ,both free and total, during the course of illness and it was assumed to be an important parameter in the recovery process[42]. Roca et al reported that the serum levels of FreeT4, FreeT3, and total T3 and T4 were increased on the day of hospitalization and decreased thereafter[43]. TSH levels were normal in their study

population. The authors assumed that the increased T4 levels could be due to the secretion from the thyroid gland itself.

Walch et al reported a single case study of a twenty six year old male with chronic undifferentiatied schizophrenia who was also suffering from severe hypothyroidism and noncompliant on thyroxine medications. Enhanced compliance by weekly supplementation of levothyroxine sodium led to decreased hopsitalisations and increased drug adherence with neuroleptics[44].

Serum levels of T4, T3 and TSH were evaluated in 31 patients with schizophrenia before and after four weeks of treatment with the phenothiazine derivative perazine, in a study by Baumgartner et al. The study found out that higher the level of T4, higher is the disease severity and the better is the response to the antipsychotic treatment[45].

Sim et al estimated the prevalence and the types of thyroid dysfunction in a group of 189 adult patients with chronic schizophrenia. The study reported a high prevalence (36.4%) of thryoid function test abnormalities and increased levels of Free T3 and Free T4 were found in patients who scored higher in the disease severity[46]. The patients who had thyroid dysfunction on laboratory measurements were found to be euthyroid on clinical assessment. Hence cautious interpretation of thyroid

function measures in chronic schizophrenia is advisable. No correlation with neuroleptic treatment was found in the study[46].

Yazici et al evaluated the relationship between Thyrotropin-releasing hormone test (TRH test) and the symptom dimensions and the predictive value of this test in short term outcome of schizophrenia. The results obtained implicated that higher basal TSH levels were associated with poor treatment response[47]. A better response to treatment was predicted by higher total and free T3 levels and also a bunted TSH response to TRH[47].

A prospective study was conducted in treatment resistant schizophrenics who were randomized to receive treatment with any one of Quetiapine, Risperidone and Fluphenazine for a period of six weeks. A significant decrease in total T4 fraction was observed in patients receiving Quetiapine for treatment[48]. No significant variation occurred in treatment arms with Risperidone and Fluphenazine[48].

Another study by Jose j et al assessed the association between thyoid hormones and the severity of psychopathology and suicide risk in drug free schizophrenia patients. Suicidal ideation was more in patients with higher free T4 measures, but the study did not find amy significant association between disease severity and the hormonal measurements[49].

Thyroid hormones were investigated in the role of biological markers and any possible association with symptomatology and extrapyramidal side effects analysed. Free T3 predicted significant changes in MMSE scores and was concluded that free T3 levels may be associated with better cognition and lesser extrapyramidal side effects in chronic schizophrenia[50].

In a naturalistic study aimed at evaluating the biological factors in suicidal attempters in schizophrenia, the authors found out that significant difference between suicide attempters and non attempters were seen in Free T3 levels. Suicidal attempters were likely to have lower free T3 values than non attempters[51]. The study postulated that thyroid hormones can play a crucial role in the compensatory mechanisms targeted at correcting the reduced central serotonin activity[51].

The prevalence of thyroid hormone abnormalities in long term care patients referred to psychiatry was also conducted. Elevated TSH in the sample was associated with female gender and a tendency for psychotic symptoms[52].

In an Indian study carried out in Bangalore, abnormal thyroid hormonal status was seen in 29.3% of the schizophrenia patients. The presence of hypothyroidism was seen in 25.17% and hyperthyroidism in 4.08% of the same sample[53]. These rates were almost comparable to

the rates in affective disorders (21.62% and 1.62% respectively for hypo and hyperthyroidism). Eleven of the eighteen patients with anti Thyroid Peroxidase antibody positivity had one of the schizophrenia spectrum disorders. The findings reiterate the relevance of thyroid screening in schizophrenia spectrum disorders also[53].

Case reports of schizophrenic patients responding well to large doses of T3 were also published[54]. But the statistical significance or analysis of these reports were not done. Such reports also mentioned that schizophrenia patients should be investigated for any thyroid dysfunction and if present, thyroid hormone supplementation should be included in the treatment regimen[54].

The overall analysis of all the studies done, points towards a dynamic relationship between thyroid and schizophrenia.

ASSOCIATION BETWEEN THYROID HORMONES AND NEUROTRANSMITTERS

1. DOPAMINE

Dopamine was the first neurotransmitter found to have an association in schizophrenia due to the fact that antipsychotics with D2 receptor blockade are helpful in reducing the symptoms[55]. Thyroid hormones are known to modulate the levels of Dopamine receptors and

the activity of the enzyme tyrosine hydroxylase, which is the rate limiting enzyme in catecholaminergic pathway[56-58]. On the other hand, dopamine is found to reduce TSH secretion[59]. On treating schizophrenic patients with neuroleptics, it will cause an increase in the levels of TSH and can result in the diagnosis of subclinical hypothyroidism[60].

SEROTONERGIC SYSTEM

Serotonin is considered to be an essential neurotransmitter and is equally important in schizophrenia as dopamine. The strongest evidence for the role of serotonin in schizophrenia comes from the fact that serotonin receptors are implicated in the efficacy of atypical antipsychotics[61]. Cerebrospinal fluid was analsyed and the levels of 5HIAA (metabolite of serotonin pathway) was correlated with plasma values of thyroid hormones. The concentration of 5HIAA was significantly and negatively correlated with plasma concentrations of total T3 and TSH[62]. Diminished serotonin activity was observed in hypothyroid individuals also[63-64]. Altogether, there are clear cut findings indicating serotonin – thyroid interactions and thus a possible role in schizophrenia[65].

2. GLUTAMATERGIC SYSTEM

The current concept in schizophrenia is shifting towards a glutamatergic hypothesis ever since the observation that Ketamine and

phencyclidine, NMDA type glutamate receptor blockers induces neurocognitive deficits and psychosis similar to schizophrenia[66].

Glutamate model tells about the hypofunctionality of forebrain glutamate system[67-68].

Another study had concluded that T3 modulated the astrocyte glutamate receptors and facilitated neuronal protection and development[69]. Glutamate and other excitatory neurotransmitters can modulate the secretion of anterior pituitary hormones like TSH and plays a role in neuroendocrine regulation of Hypothalmic - pituitary axis[70-72].

3. GABA NEUROTRANSMISSION

The probablity that thyroid hormones influence the GABAergic system was first hypothesised in the 1960s. Following it, multiple studies have analysed this association.

The influence of the thyroid hormones in the GABAergic neurotransmission happens at varied stages including circuit formation, enzymes involved in the production of GABA and its metabolism, GABA receptors and GABA release and reuptake[73]. Animal studies has shown that there is decreased activity of the enzymes involved in metabolism of GABA in hypothyroid animals[74]. In such animals, when T3

replacement was given, the activity of the enzymes reverted to normal[75].

Analysis of the studies suggests that, the existence of correlation found in some studies between thyroid hormones and GABAergic function is not a consistent finidng across studies[76].

4. MYELINATION AND CYTOKINES

The thyroid hormones are involved in regulating the process of myelination and the functioning of oligodendrocytes. These two processes are considered as crucial in regulating the neural systems and is of special mention in schizophrenia where there is evidence for white matter tract involvement[78-79].

THE NEUROTRANSMITTER ROLE OF THYROID HORMONES

The role of T3 as a neurotransmitter has been proposed[80]. This is based on the localisation between thyroid hormones and noradrenergic system[81]. T3 also gets stored inside the nerve endings and secreted with the help of a calcium dependent mechanism[82-84]. In this context, the role of thyroid hormones in schizophrenia has to be evaluated.

The existing data analysis shows that there is a need for screening patients with schizophrenia for assessing their thyroid hormonal status.

AIMS AND OBJECTIVES

AIM:

The current study attempts to estimate the prevalence of thyroid dysfunction in patients with schizophrenia and to assess the correlation between thyroid hormone levels and the severity of psychopathology in them.

OBJECTIVES

PRIMARY OBJECTIVE:

1. To estimate the prevalance of thyroid dysfunction in patients with schizophrenia.

2. To assess the correlation between levels of thyroid hormones and the severity of psychopathology.

SECONDARY OBJECTIVE:

1. To estimate the correlation between illness characteristics & thyroid hormone levels.
2. To compare the severity of psychopathology between patients with schizophrenia with & without thyroid dysfunction
3. To assess the prevalance of thyroid dysfunction in various subtypes of Schizophrenia
4. To compare the thyroid hormone levels between the various diagnostic subgroups of schizophrenia.

NULL HYPOTHESIS

1. There is no relationship between the thyroid hormone levels and the severity of psychopathology in patients with schizophrenia.

2. There is no relationship between the positive symptoms score in the Positive And Negative Syndrome Scale (PANSS) and the thyroid hormone levels in patients with schizophrenia.

3. There is no relationship between the negative symptoms score in PANSS and the thyroid hormone levels in patients with schizophrenia.

4. There is no relationship between the general psychopathology score in PANSS and thyroid hormone levels in patients with schizophrenia.

MATERIALS AND METHODS

Section A: Sample Selection:

The present study is a cross sectional study conducted at the Institute of Mental Health, Rajiv Gandhi Government General Hopsital, Chennai. The participants were one hundred patients with Schizophrenia who were selected from the outpatient department of Institute of Mental Health.

Inclusion Criteria:

1. Patients with Schizophrenia diagnosed as per ICD 10 criteria

2. Age between 18 – 40 yrs

3. Who are giving written informed consent

Exclusion Criteria:

1. Mental Retardation
2. H/o any other psychiatric illness ruled out using SCAN
3. H/O thyroid disorder previously
4. H/O lithium treatment or other medications like propranolol, metformin use which are known to impair thyroid function.
5. H/O concurrent neurological illness or systemic illness known to impair thyroid function.
6. H/o substance dependence
7. Pregnancy

Section B: Instruments used

Clinical Assessments

I. Socio-demographic data sheet

A structured proforma was used to elicit information about the demographic details and illness characteristics of the patients with schizophrenia.

II. Schedules for Clinical Assessment In Neuropsychiatry, SCAN (WHO,1999)[85].

Schedules for clinical assessment in neuropsychiatry are manuals made by the World Health Organisation (WHO) for the purpose of assessing, measuring and classifying mental illnesses. It can be used in varied settings like in clinical and research settings. The stability and validity of this schedule has been proved in multiple studies.

SCAN is a semi structured and clinical interview schedule. It has got the provision for cross examination of the individual. There is no order by which the interview should proceed, thus making this instrument a flexible one. The schedule is divided into various sections and each section carries certain significant questions pertaining to that section. If these questions are answered positively, then the questions beneath the cut-off point are also asked to the patient.

III. Positive And Negative Syndrome Scale (PANSS)[86]

The PANSS developed by S R Kay et al, is used to assess symptoms in schizophrenia and it finds its use both clinically and in research studies. It is a 30 item rating scale created on the basis that schizophrenia has two distinct symptom profiles namely the positive and the negative symptoms. The patient is rated on a 1 to 7 rating scale on 30 different symptoms which includes positive, negative and general psychopathology. PANSS roughly takes about 40 minutes to complete.

IV. LABORATORY MEASUREMENT OF THYROID HORMONES

The laboratory analysis of thyroid hormones was done by using the Electro- Chemiluminescence Immuno Assay Method (eclia). This method is based on the luminescence generated by electrochemical reactions in solutions. This assay is considered as a highly superior method in terms of sensitivity and is used in analytical research[87-88].

In this technique, the electrochemiluminescence quality is integrated into the conventional Antigen- Antibody reactions. These reactions take place on the surface of a streptavidin coated paramagnetic microparticle during two incubations. The incubation time varies depending on the assays.

This technique generally uses Ruthenium complexes, regenerating with Tripropylamine in liquid phase or liquid-solid interface. In the first step, a patient sample is combined with a reagent containing biotinylated TSH antibody and a second Ruthenium conjugated TSH antibody in an assay cup. During the incubation period, the antibodies capture the TSH present in the sample. Next, the sample solution is drawn into the ECL measuring cell along with a buffer solution containing tripropylamine. A magnet located under the electrode captures the microparticles in a thin, even layer on the electrode's surface.

Liquid flow rinses away all unbound reagent and sample. This is the bound/free separation process. The magnet is removed and voltage is applied to the electrode. Two oxidation reactions are simultaneously initiated, resulting in the oxidation of the ruthenium complex and the TPA in the solution.

The two compounds react to produce an excited state of the ruthenium conjugate .Spontaneous decay results in the emission of a photon of light at 620 nm. Multiple readings are taken by a Photomultiplier Tube (PMT) and the readings are intergrated into a single value and compared with a calibration curve to obtain the test sample result. Similarly the values of Free T3 and Free T4 are also deducted for the test sample.

The normal values of the Thyroid Function Profile by the test used in the present study is

Free T3 : 2.0-4.4 pg/ml

Free T4 : 0.8-2.0 ng/dl

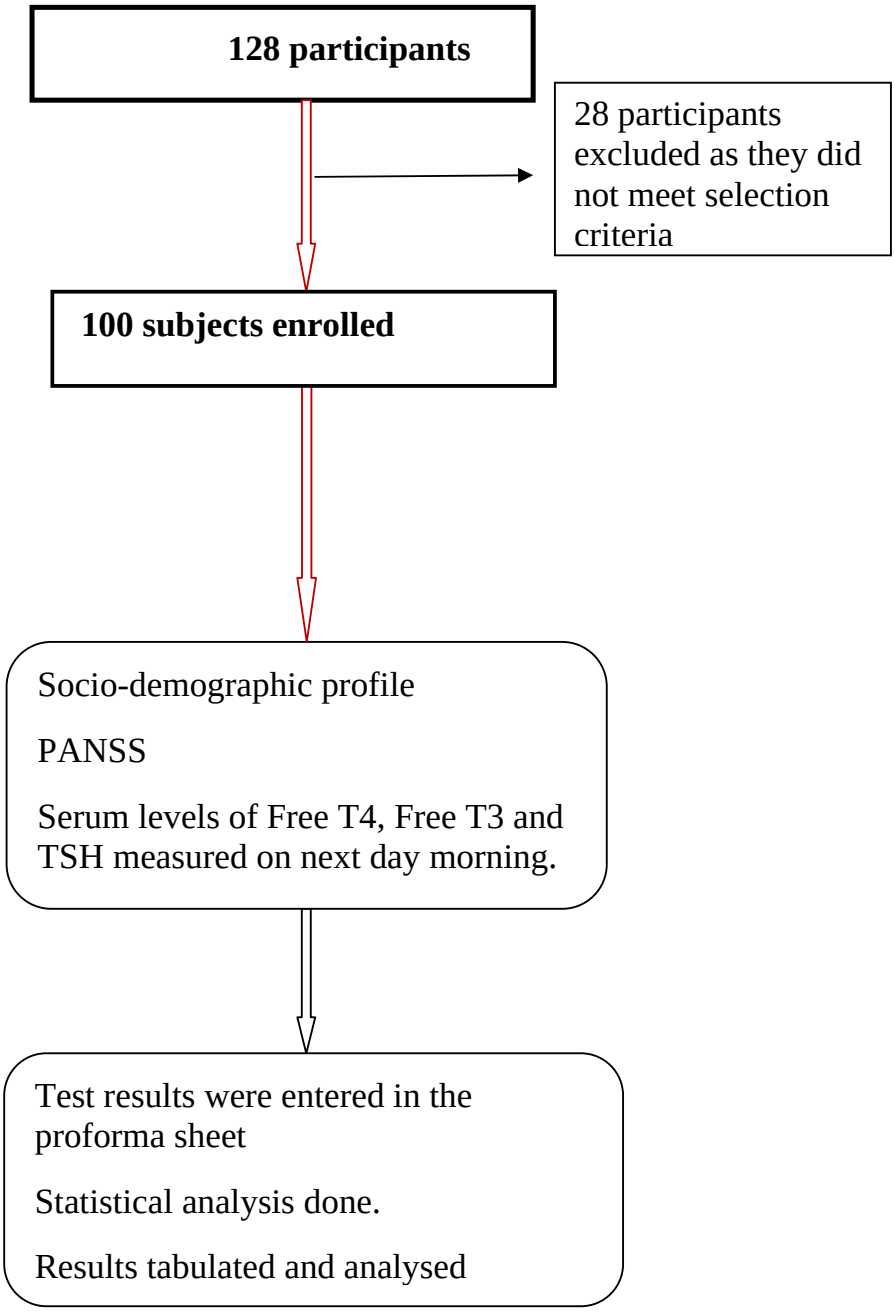
TSH : 0.35-5.50 mIu/ml.

Thyroid dysfunction was defined as values of the thyroid hormones lying outside the normal range and subjects were divided into those with various thyroid disorders. Those with normal Free T3 and Free T4, but with raised TSH were diagnosed with subclinical hypothyroidism. Those with high or normal values for Free T3 and Free T4 and low values for TSH were diagnosed with primary hyperthyroidism, and those with low values for Free T3 and Free T4, high values for TSH were diagnosed with primary hypothyroidism[89]. A normal free T3 and T4 along with normal TSH was considered to be normal thyroid status[89-90].

METHODOLGY OF SELECTION AND LABORATORY ASSESSMENT

The subjects for the study were selected from the outpatient department of Institute of Mental Health, Madras Medical College, Chennai. The subjects who satisfied the inclusion and exclusion criteria were selected for the study. After selection, the subjects were explained about the study and written informed consent was obtained from them before the start of the study. The PANSS scoring done and details in the socio demographic data sheet were collected on the day of including the subjects for the study. The thyroid hormones were measured in the serum by collecting venous blood, in a fasting state on the next day morning. The test results were also entered in the proforma as soon as they were obtained.

METHODOLOGY FLOW CHART



DATA ANALYSIS

The results were tabulated and analyzed using the statistical package SPSS 22.0.

Descriptive statistics was used to obtain the mean and standard deviations with respect to different variables of socio-demographic profile and the illness characteristics of the study population. Pearson correlation was used to assess the relationship between severity of psychopathology and thyroid hormones.

Scatter diagram was used to represent the correlation between the severity of psychopathology and thyroid hormone levels.

T –test was used to compare the mean values of thyroid hormones between male and female gender. The mean values of thyroid hormones were compared between the diagnostic subgroups of schizophrenia by using ANOVA. Comparison of the proportion of thyroid dysfunction between diagnostic subgroups of schizophrenia was done by using chi square test.

RESULTS

The current study is a cross sectional study. One hundred subjects were enrolled in the present study. The subjects were selected from the outpatient department, Institute of Mental Health, Madras Medical College, Chennai.

Socio-demographic data :

Age:

Table 1: Descriptive Statistics for age

N	100
Mean	33.19
Median	35.00
Std. Dev	6.115
Minimum	19
Maximum	40

The above table shows the descriptive statistics for the age. The mean age of the sample was 33.19 ±6.115. The minimum age of the study population obtained was 19 and the maximum was 40.

Table 2. Frequency table of age distribution

Age group	N	%
< 25 yrs	16	16.0
26 - 30 yrs	19	19.0
31 - 35 yrs	21	21.0
36 - 40 yrs	44	44.0
Total	100	100.0

The above table shows the proportion of the sample in each of the age groups. 44% of the study population belonged to the age group of 36-40yrs. 16% of the sample were in the age group of less than 25yrs.

Gender:

Table 3. Gender distribution of the sample

GENDER	N	%
Male	41	41.0
Female	59	59.0
Total	100	100.0

The total number of males in the sample was 41 while the number of females in the sample was 59.

Chart 1: Pie chart for the distribution of age in the sample

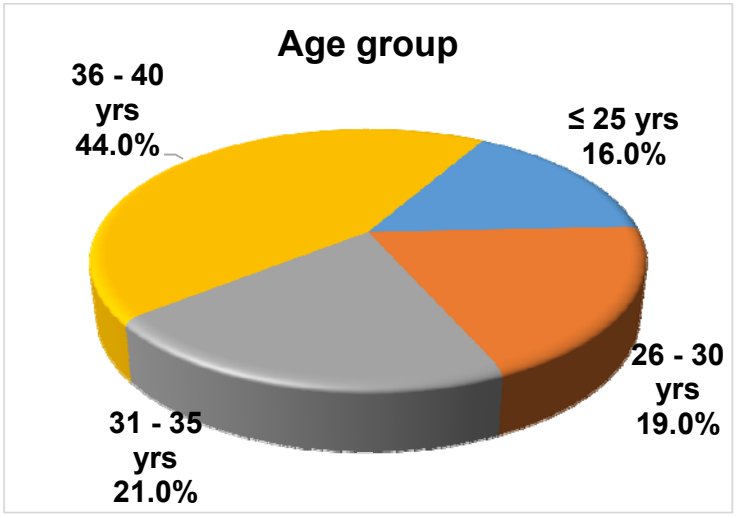


Chart 2: Pie chart for Gender distribution of the sample

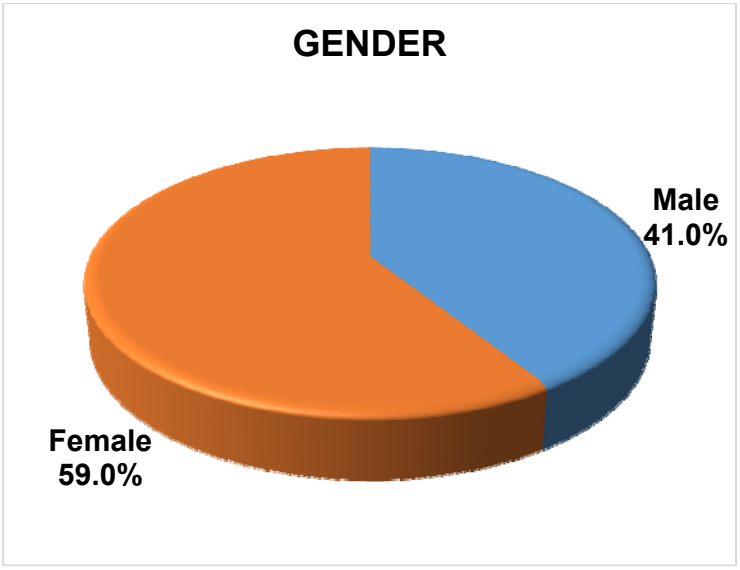


Table 4: Education status of the sample

EDUCATION	N	%
Profession or honours	0	.0
Graduate or Post graduate	7	7.0
Intermediate or diploma	17	17.0
High school	32	32.0
Middle school	16	16.0
Primary school	16	16.0
Illiterate	12	12.0
Total	100	100.0

The above table shows the education level of the study population.

Chart 3: Pie Chart showing education level of the study population

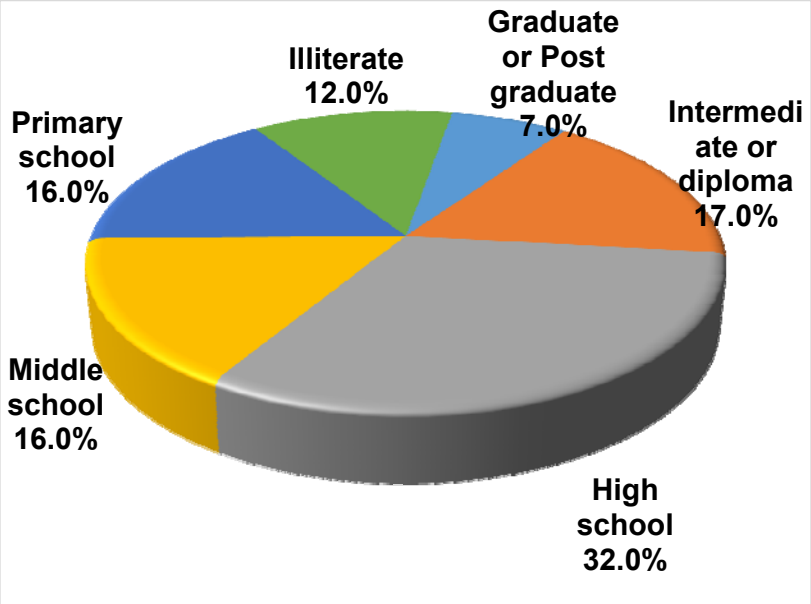


Table 5: Occupation of the study population

OCCUPATION	N	%
Profession	0	0
Semi- profession	1	1.0
Clerical, shop –owner, farmer	5	5.0
Skilled worker	10	10.0
Semi-skilled worker	19	19.0
Unskilled worker	28	28.0
Unemployed	37	37.0
Total	100	100.0

The above table shows the occupation of the study population.

Chart 4: Pie Chart showing the occupation of the study population

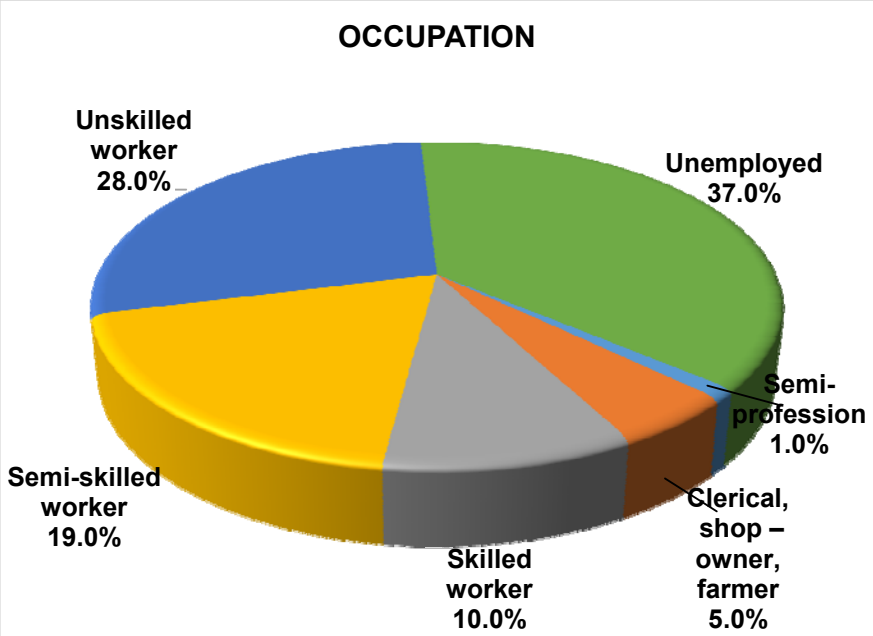


Table 6: Socio-economic status of the study population

SES	N	%
Upper	0	.0
Upper middle	1	1.0
Lower middle	19	19.0
Upper lower	70	70.0
Lower	10	10.0
Total	100	100.0

The above table shows the socio-economic status of the study population

Chart 5: Pie chart showing socio-economic status of the study population

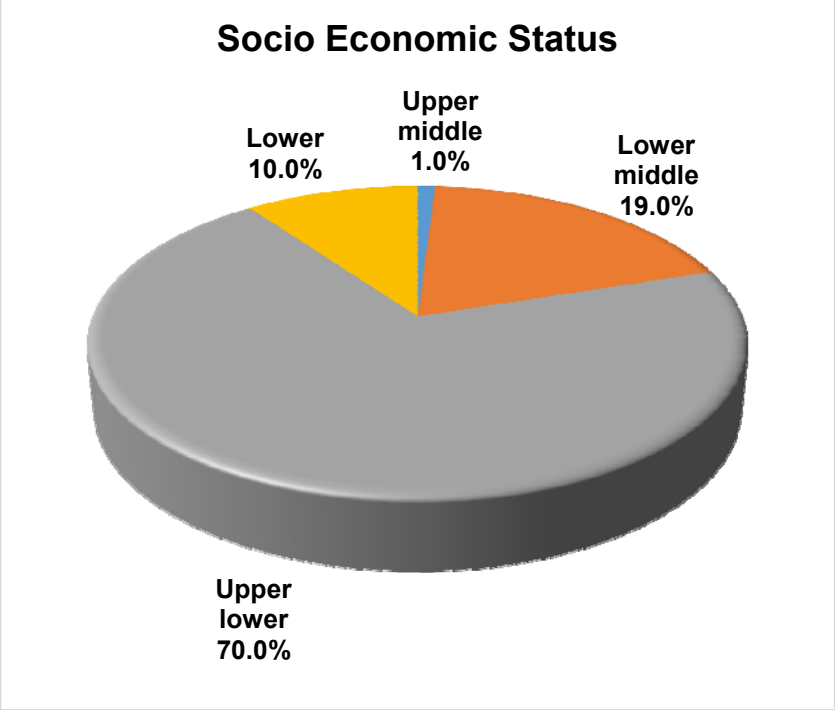


Table 7: Locality of the study population

RESIDENCE	N	%
Urban	63	63.0
Semi urban	17	17.0
Rural	20	20.0
Total	100	100.0

The above table shows the residence of the study population. 63% were residing in the urban locality and 20% of the study population resided in the rural locality.

Table 8: Marital Status of the study population

MARITAL STATUS	N	%
Married	70	70.0
Divorcee	6	6.0
Single	24	24.0
Total	100	100.0

The above table shows the marital status of the study population. 70% of the subjects were married while 24% of the subjects were unmarried. 6% of the subjects were divorced.

Table 9: Religion of the study population

RELIGION	N	%
Hindu	78	78.0
Christian	16	16.0
Muslim	6	6.0
Others	0	.0
Total	100	100.0

The above table shows the religion followed by the subjects. 78% of the study population followed Hinduism, 16% followed Christianity and 6% of the study population were Muslims.

Table 10: Family type of the study population

FAMILY TYPE	N	%
Joint	21	21.0
Nuclear	79	79.0
Total	100	100.0

The above table shows the family type of the study population.

Table 11: Illness characteristics of the study population

Illness Characteristics	N	Mean	Std. Dev	Median	Min	Max
DURATION OF ILLNESS (MONTHS)	100	63.59	53.52	48.00	2.00	240.00
AGE AT ONSET (YRS)	100	27.81	5.80	28.00	15.00	38.00
DUP (MONTHS)	100	28.03	27.60	24.00	.00	180.00
DOT (MONTHS)	100	31.52	50.10	6.00	.00	216.00
PANSS POSITIVE	100	20.86	3.59	20.00	12.00	32.00
PANSS NEGATIVE	100	18.49	4.08	18.00	7.00	30.00
PANSS GEN PSY	100	30.97	5.50	31.00	16.00	48.00
PANSS TOTAL	100	70.31	9.09	70.00	46.00	97.00

The mean age of onset of illness in the study population was 27.81 ±5.80. The mean duration of the illness is 63.59 ±53.52 months. The mean duration of untreated psychosis was 28.03±27.60. Some of the subjects were on treatment with antipsychotics at the time of including in the study. The mean duration of treatment in the study population was 31.52±50.10. The severity of psychopathology was assessed with PANSS. The mean positive and negative score in the PANSS was 20.86± 3.59 and 18.49±4.08 respectively. The mean general psychopathology score was 30.97±5.50. The mean total PANSS score was 70.31±9.09.

Table 12: Mean values of FreeT3, FreeT4 and TSH in the sample

	GENDER	N	Mean	Std. Dev	t-Value	P-Value
FREE T3(pg/ml)	**Male**	41	2.5439	.40977	.374	.709
	Female	59	2.5127	.41081		
FREE T4 (ng/dl)	**Male**	41	1.6246	.46739	1.649	.102
	Female	59	1.4607	.50360		
TSH (mIu/ml)	**Male**	41	4.00615	2.002189	0.815	.417
	Female	59	4.34946	2.118837		

Significance $p<0.05$

The above table shows the mean serum values of thyroid hormones in males and females separately. The mean Free T3 value in males was 2.5439±0.40977 and that in females was 2.5127±0.41081. The mean Free T4 value in males was 1.6246±0.46739 and in females was 1.4607±0.50360. The mean TSH value in males was 4.00615±2.002189 and that in females was 4.34946±2.118837. Comparison of the mean values between females and males was done by using T-test.

There was no significant difference in the mean values of Free T3, Free T4 and TSH between the two genders ($p>0.05$).

Table 13: Distribution of Diagnostic subgroups in the study population

TYPE OF SCHIZOPHRENIA	N	%
Paranoid	77	77.0
Hebephrenic	3	3.0
Undifferentiated	20	20.0
Total	100	100.0

The study population consisted of 77% of the subjects with a diagnosis of Paranoid schizophrenia, 20% with a diagnosis of Undifferentiated schizophrenia and 3% of Hebephrenic schizophrenia.

Table 14: Distribution of Treatment Received in the study population

TREATMENT RECEIVED	N	%
Untreated	51	51.0
Haloperidol	23	23.0
Risperidone	12	12.0
Olanzapine	14	14.0
Total	100	100.0

The above table shows the distribution of treatment received in the study population. 51% of the study population was untreated. 23% of the study population received treatment with Haloperidol at the time of enrolling in the study. 12 % of the study population was on treatment with Risperidone and 14% was on treatment with Olanzapine at the time of including in the study.

Chart : Pie Chart showing distribution of treatment in the study population

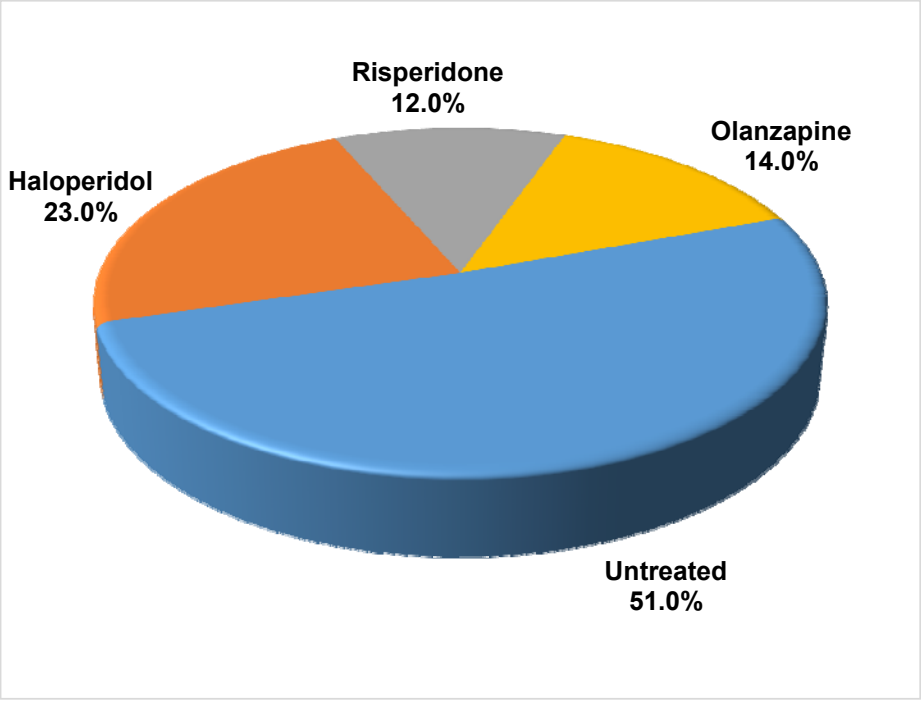


Table 15: Distribution of Abnormal thyroid hormone values in the sample

		N	%
Free T3	Normal	100	100.0
	Abnormal	0	.0
	Total	100	100.0
Free T4	Normal	97	97.0
	Abnormal	3	3.0
	Total	100	100.0
Free TSH	Normal	73	73.0
	Abnormal	27	27.0
	Total	100	100.0

The table above shows the distribution of abnormal thyroid hormone values in the study population. Abnormal values of Free T4 was found in 3 % of the sample. Abnormal values of TSH was found in 27% of the study population. The values of Free T3 in the sample was lying within the normal range.

Table 16: Distribution of Thyroid Disorder in the sample

Thyroid Disorder		N	%
Subclinical hypothyroidism	Yes	25	25.0
	No	75	75.0
	Total	100	100.0
Primary hypothyroidism	Yes	0	.0
	No	100	100.0
	Total	100	100.0
Hyperthyroidism	Yes	0	.0
	No	100	100.0
	Total	100	100.0

The above table shows the prevalence of thyroid disorder in the study population. The prevalence of subclinical hypothyroidism in the study population was 25%. Primary hypothyroidism and hyperthyroidism was not present in the sample.

Table 17: Table showing correlation between PANSS total score and thyroid hormone measurements

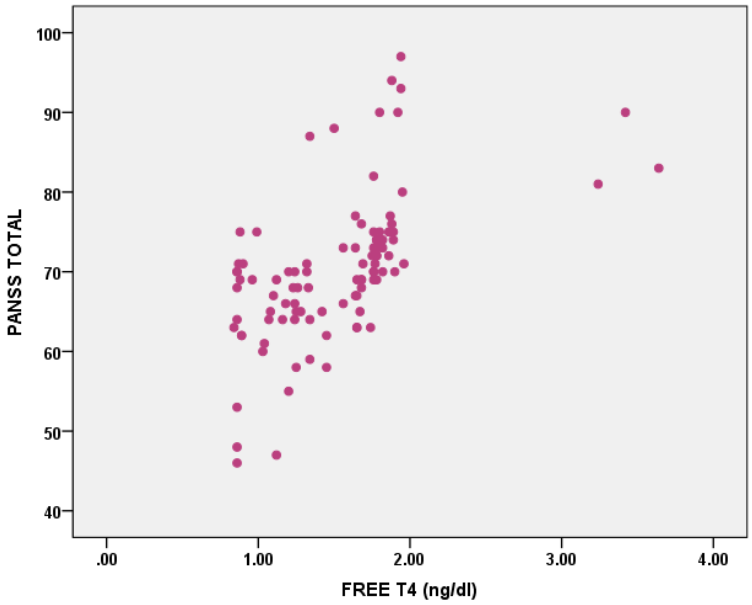
		PANSS TOTAL
FREE T3(pg/ml)	Pearson Correlation	.092
	P-Value	.365
	N	100
FREE T4 (ng/dl)	Pearson Correlation	.579
	P-Value	<0.001
	N	100
TSH (mIu/ml)	Pearson Correlation	.104
	P-Value	.305
	N	100

Significance $p<0.05$

The table above shows the correlation between the PANSS total score and the values of Free T3, Free T4 and TSH. A significant correlation was obtained between the PANSS total score and the Free T4 values (Pearson correlation= 0.579 and $p<0.001$). There was no significant correlation between the PANSS total score and Free T3 and TSH values ($p>0.05$).

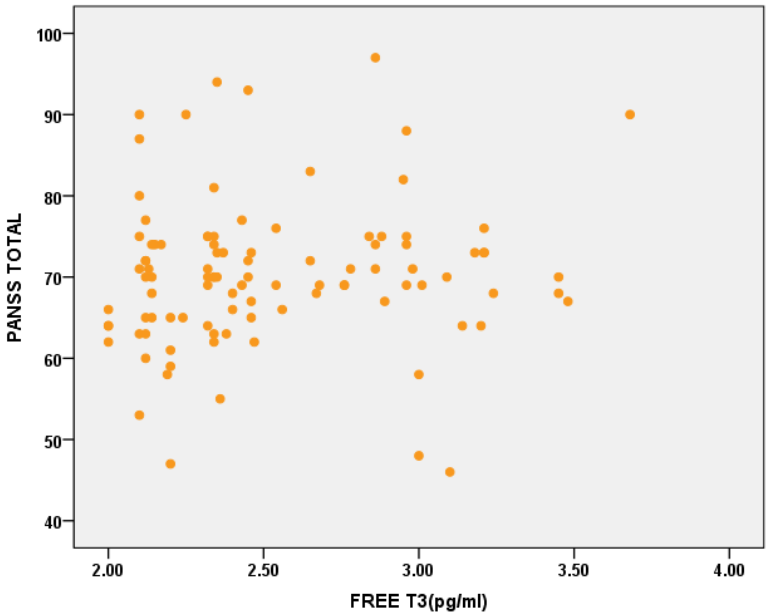
Scatter Diagram showing the correlation between

PANSS total score and Free T 4.



Scatter Diagram showing correlation between

PANSS total score and Free T3



Scatter diagram showing correlation between PANSS total score and TSH

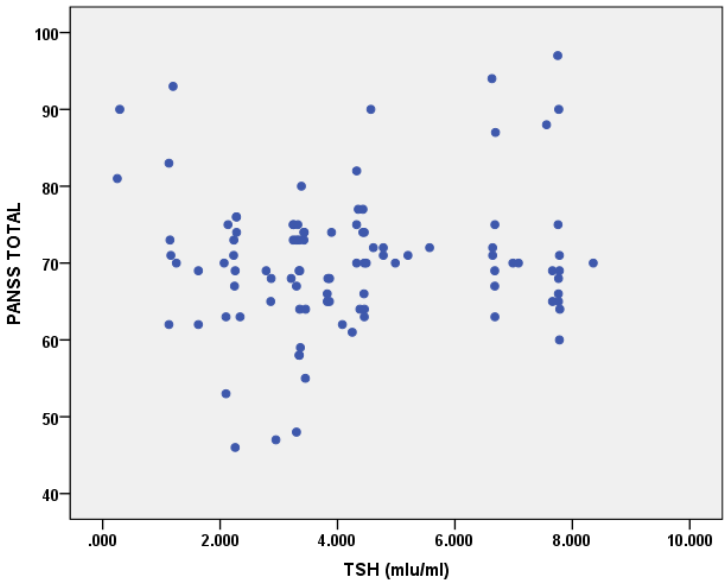
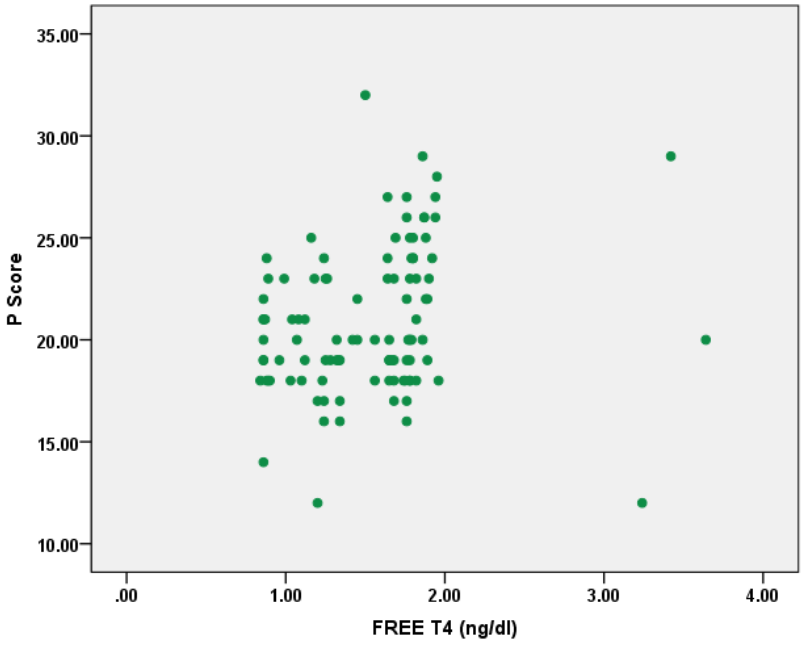


Table 18: Correlation between the Positive, Negative and General psychopathology scores in PANSS and thyroid hormones

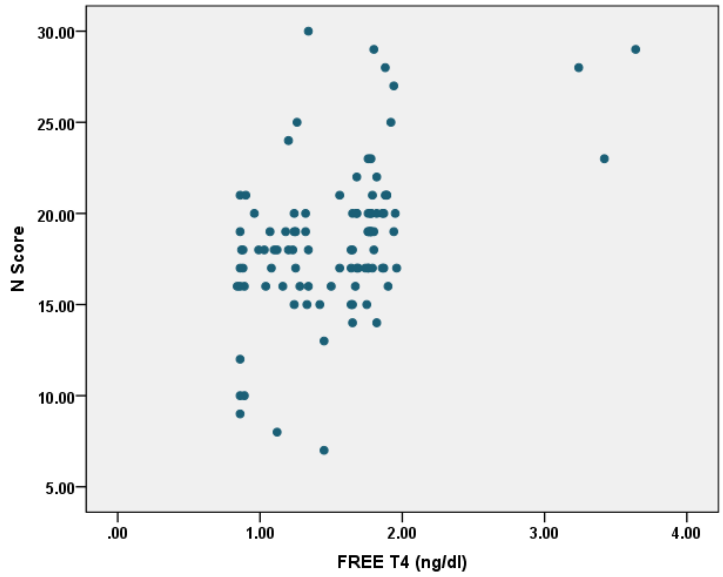
		P Score	N Score	G Score
FREE T3(pg/ml)	Pearson Correlation	.172	.027	.021
	P-Value	.087	.789	.836
	N	100	100	100
FREE T4 (ng/dl)	Pearson Correlation	.210	.470	.469
	P-Value	.036	<0.001	<0.001
	N	100	100	100
TSH (mIu/ml)	Pearson Correlation	.062	.082	.080
	P-Value	.540	.415	.426
	N	100	100	100

The above table shows the correlation between the positive, negative, and general psychopathology scores in PANSS and the thyroid hormone measures. There was a significant positive correlation between the positive, negative and general psychopathology scores and the Free T4 values ($p<0.05$). There was no significant correlation between the positive, negative and general psychopathology scores and the Free T3 and TSH values ($p>0.05$).

Scatter diagram showing the correlation between Positive symptoms score in PANSS and Free T4 values



Scatter Diagram showing the correlation between the Negative symptoms scores in PANSS and the Free T4 values



Scatter Diagram showing the General Psychopathology scores in PANSS and the Free T4 values

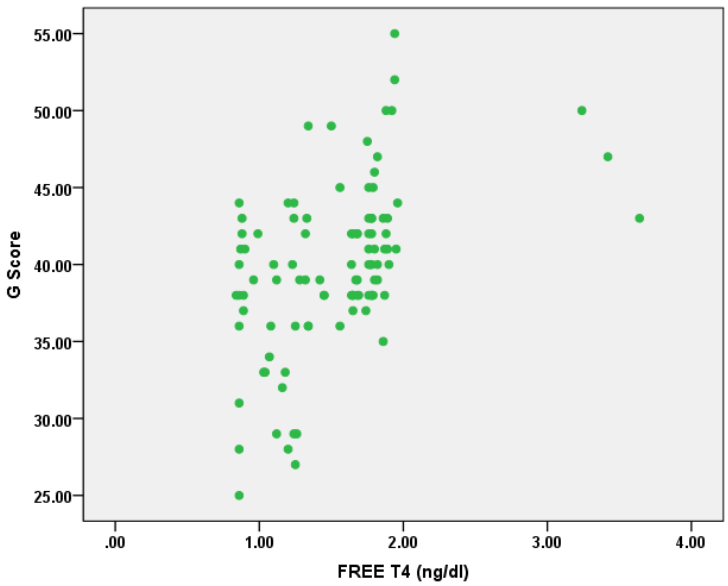


Table 19:Correlation between each of the

Positive symptoms and thyroid hormones

		FREE T3 (pg/ml)	FREE T4 (ng/dl)	TSH (mIu/ml)
P1 Delusions	Correlation	.122	.143	-.039
	P-Value	.225	.156	.697
	N	100	100	100
P2 Conceptual disorganisation	Correlation	.126	.062	.038
	P-Value	.211	.541	.704
	N	100	100	100
P3 Hallucinatory behaviour	Correlation	.060	.026	.064
	P-Value	.556	.797	.528
	N	100	100	100
P4 Excitement	Correlation	.151	.311	-.050
	P-Value	.134	.002	.622
	N	100	100	100
P5 Grandiosity	Correlation	.055	.106	.084
	P-Value	.585	.293	.407
	N	100	100	100
P6 Suspiciousness	Correlation	.138	.152	-.018
	P-Value	.171	.132	.858
	N	100	100	100
P7 Hostility	Correlation	-.001	.042	.109
	P-Value	.988	.677	.279
	N	100	100	100

Table 20: Correlation between each of the Negative symptoms and thyroid hormones

		FREE T3(pg/ml)	FREE T4 (ng/dl)	TSH (mIu/ml)
N1 Blunted affect	Correlation	.038	.429	-.055
	P-Value	.710	<0.001	.590
	N	100	100	100
N2 Emotional withdrawal	Correlation	.073	.390	-.011
	P-Value	.468	<0.001	.911
	N	100	100	100
N3 Poor rapport	Correlation	.014	.102	.110
	P-Value	.891	.314	.278
	N	100	100	100
N4 Passive/apathetic social withdrawal	Correlation	-.111	.288	.154
	P-Value	.271	.004	.126
	N	100	100	100
N5 Difficulty in abstract thinking	Correlation	.136	.147	.126
	P-Value	.176	.144	.210
	N	100	100	100
N6 Lack of spontaneity & flow of conversation	Correlation	-.036	.425	.024
	P-Value	.720	<0.001	.814
	N	100	100	100
N7 Stereotyped thinking	Correlation	-.013	.220	.025
	P-Value	.898	.028	.807
	N	100	100	100

Table 21: Correlation between each of the general psychopathology scores and thyroid hormones

		FREE T3(pg/ml)	FREE T4 (ng/dl)	TSH (mIu/ml)
G1 Somatic concern	Correlation	.123	.260	-.133
	P-Value	.225	.009	.186
G2 Anxiety	Correlation	.002	.205	.051
	P-Value	.984	.041	.611
G3 Guilt feelings	Correlation	.217	.252	-.092
	P-Value	.030	.012	.361
G4 Tension	Correlation	.120	.106	.043
	P-Value	.235	.295	.671
G5 Mannerisms & posturing	Correlation	-.095	.155	.003
	P-Value	.346	.123	.975
G6 Depression	Correlation	.094	.296	-.183
	P-Value	.352	.003	.068
G7 Motor retardation	Correlation	-.041	.233	-.203
	P-Value	.685	.020	.043
G8 Uncooperativeness	Correlation	-.084	-.069	.278
	P-Value	.407	.493	.005
G9 Unusual thought content	Correlation	.161	.288	.220
	P-Value	.108	.004	.028
G10 Disorientation	Correlation	.003	.153	-.134
	P-Value	.973	.129	.183
G11 Poor attention	Correlation	.032	.198	.003
	P-Value	.750	.048	.980
G12 Lack of judgement & insight	Correlation	-.022	.100	.144
	P-Value	.831	.321	.153

G13 Disturbance of volition	Correlation	.041	.254	.159
	P-Value	.688	.011	.113
G14 Poor impulse control	Correlation	-.097	.188	-.111
	P-Value	.336	.062	.270
G15 Preoccupation	Correlation	-.041	.220	.045
	P-Value	.686	.028	.660
G16 Active social avoidance	Correlation	-.113	.270	.029
	P-Value	.264	.007	.772

Table 21 contd..

The tables 19, 20 and 21 show the correlation between each of the positive, negative and general psychopathology symptoms in PANSS and the thyroid hormones. There was a significant correlation between the positive symptom of excitement and Free T4 values ($p<0.05$). There was a significant correlation between the negative symptoms of blunted affect, emotional withdrawal, social withdrawal, lack of spontaneity of conversation and stereotyped thinking with free T4 values($p<0.05$). There was a significant correlation between the general psychopathology symptoms of somatic concern, anxiety, guilt feelings, depression, unusual thought content, poor attention, disturbance of volition, pre occupation and active social avoidance with Free T4 values($p<0.05$). There was no correlation between each of the positive and negative symptoms and the

Free T3 and TSH value ($p>0.05$). There was a significant correlation between the general psychopathology symptom of guilt feelings and the Free T3 values ($p<0.05$). There was a significant correlation between the general psychopathology symptoms of motor retardation, uncooperativeness, and unusual though content and the TSH values ($p<0.05$).

Table 22: correlation between illness characteristics and thyroid hormones

		FREE T3(pg/ml)	FREE T4 (ng/dl)	TSH (mIu/ml)
DURATION OF ILLNESS (MONTHS)	Correlation	-.194	-.057	.053
	P-Value	.053	.572	.601
AGE AT ONSET (YRS)	Correlation	-.015	.113	-.086
	P-Value	.880	.261	.396
DUP (MONTHS)	Correlation	-.250	.060	.030
	P-Value	.062	.554	.769
DOT (MONTHS)	Correlation	-.120	-.073	.032
	P-Value	.235	.473	.755
	N	100	100	100

The above table shows the correlation between illness characteristics of the study population and the serum levels of thyroid hormones. No significant correlation was obtained between the duration of illness, age of onset of the illness, duration of untreated psychosis and the duration of treatment and the Free T4, Free T3 and TSH values($p>0.05$).

Table 23: Independent samples T-Test to compare mean values between TSH levels

Scores	Free TSH	N	Mean	Std. Dev	t-Value	P-Value
P Score	Normal	73	20.8904	3.37294	.138	.890
	Abnormal	27	20.7778	4.20012		
N Score	Normal	73	18.0000	3.77859	2.007	.048
	Abnormal	27	19.8148	4.60800		
G Score	Normal	73	38.8904	5.15203	2.940	.004
	Abnormal	27	42.3333	5.32772		
Total Score	Normal	73	77.7808	8.13642	2.610	.010
	Abnormal	27	82.9259	10.26168		

The above table shows the comparison of psychopathology between groups having normal and abnormal TSH levels. There was a significant difference between the two groups in PANSS total score, negative symptoms score and the general psychopathology score

(p<0.05). The scores were significantly high in groups having abnormal TSH levels. No significant difference was observed in positive symptoms score(p>0.05) between the two groups.

The comparison of psychopathology between groups having normal and abnormal Free T3 and Free T4 levels could not be done as the values of Free T3 and Free T4 were lying within the normal range.

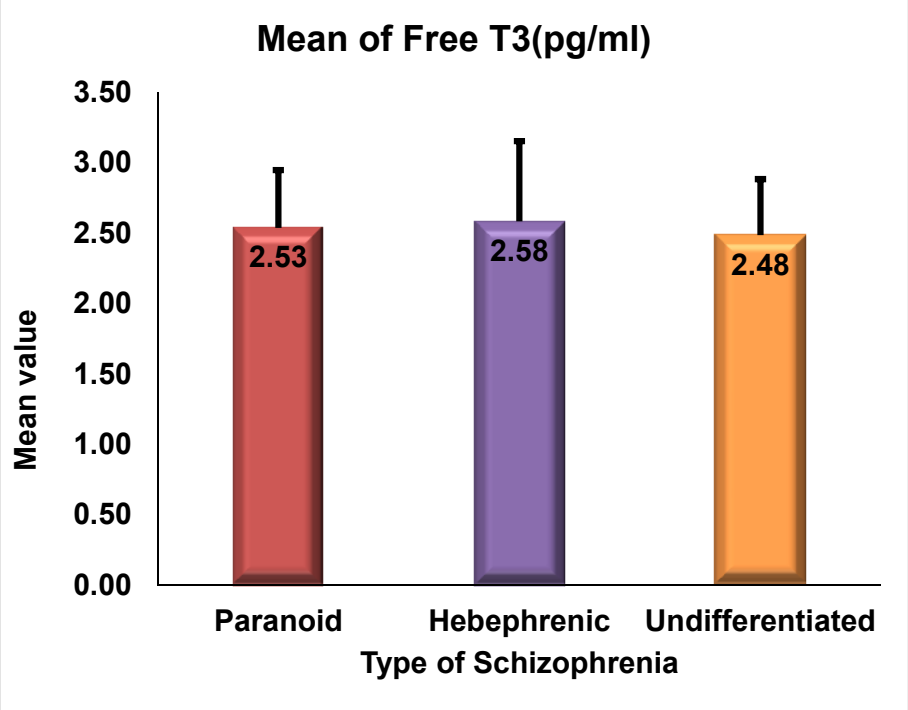
Table 24: Oneway ANOVA to compare mean values between types of Schizophrenia

Variables	Schizophrenia	N	Mean	Std. Dev	F-Value	P-Value
FREE T3(pg/ml)	Paranoid	77	2.5345	.41066	.154	.858
	Hebephrenic	3	2.5800	.57000		
	Undifferentiated	20	2.4825	.39799		
	Total	100	2.5255	.40860		
FREE T4 (ng/dl)	Paranoid	77	1.4875	.46974	1.606	.206
	Hebephrenic	3	1.4067	.47343		
	Undifferentiated	20	1.7015	.56698		
	Total	100	1.5279	.49337		
TSH (mIu/ml)	Paranoid	77	4.38549	2.134231	1.606	.206
	Hebephrenic	3	2.38733	.354865		
	Undifferentiated	20	3.80125	1.798889		
	Total	100	4.20870	2.068500		

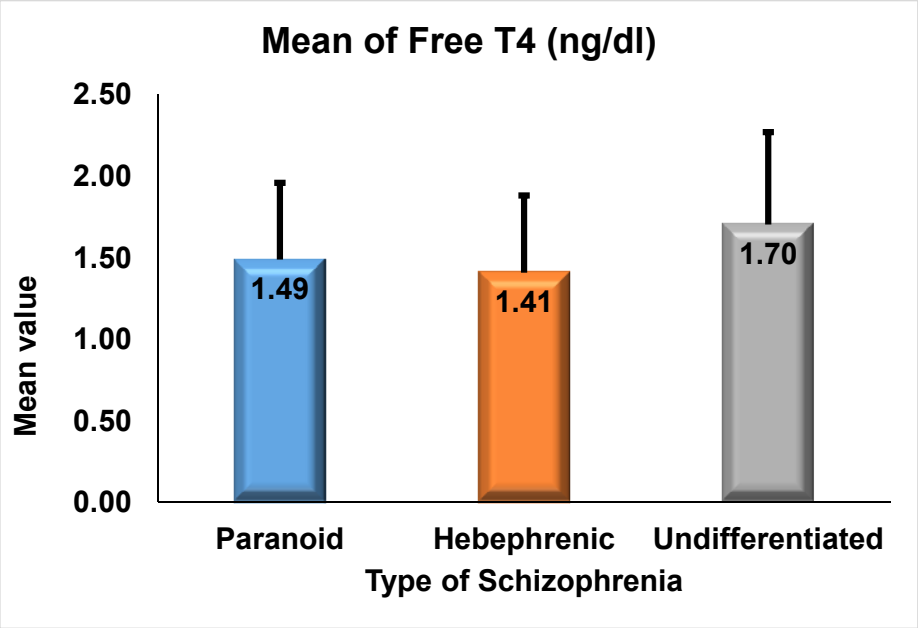
Significance P<0.05

The above table shows the comparison of mean Free T3, mean Free T4 and TSH values between the diagnostic subgroups of schizophrenia. There was no significant difference in the mean values of free T3, free T4 and TSH between the subgroups of paranoid, hebephrenic and undifferentiated schizophrenia.

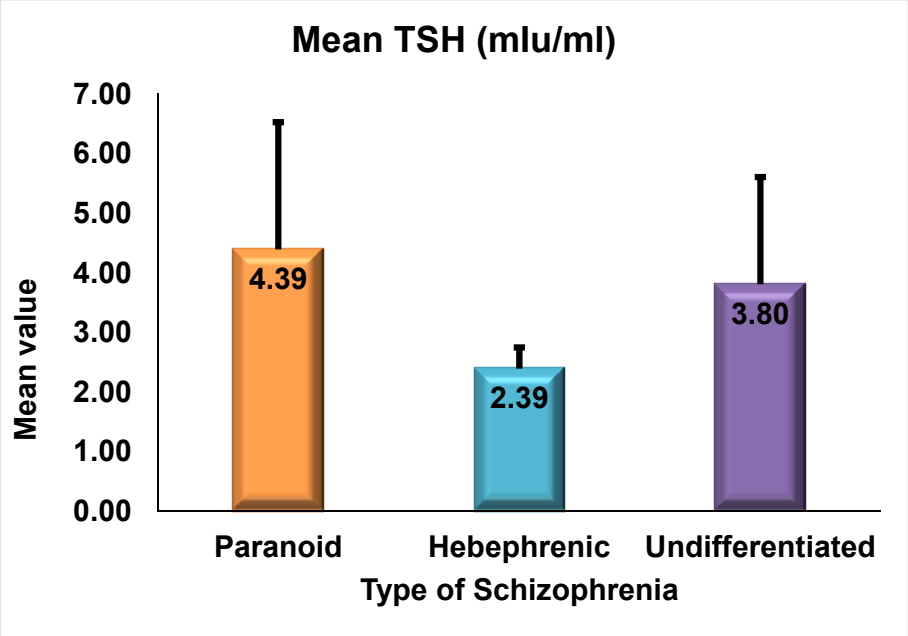
Bar diagram showing mean Free T3 values in diagnostic subgroups of schizophrenia



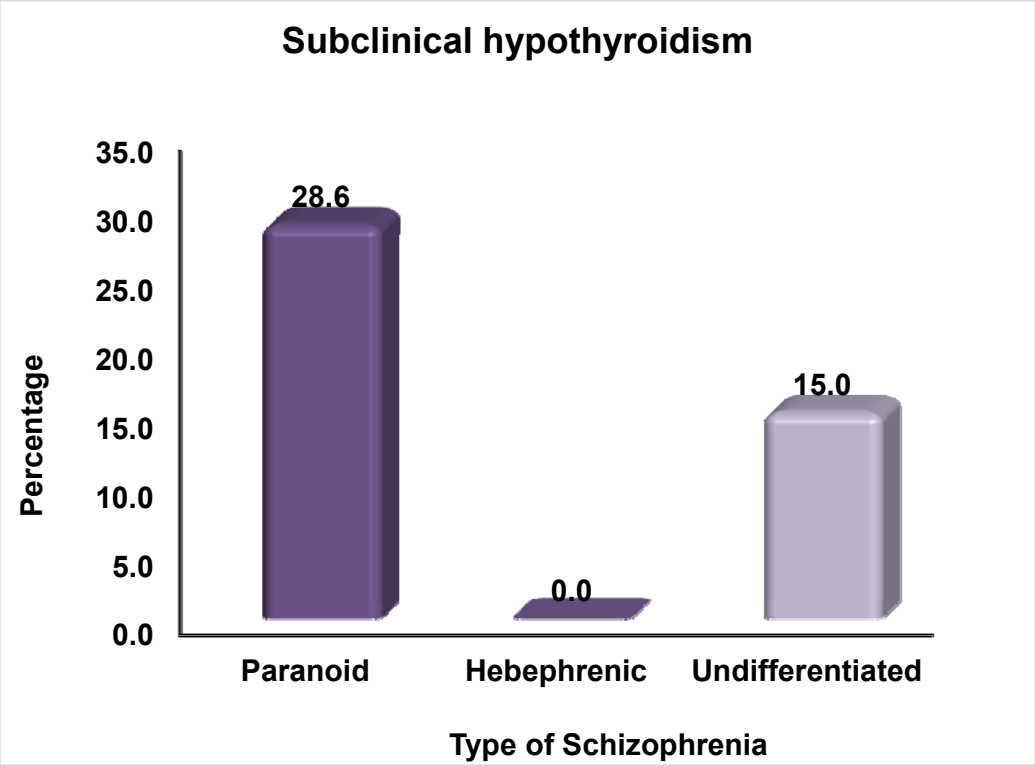
Bar diagram showing mean FreeT4 values in diagnostic subgroups of schizophrenia



Bar diagram showing mean TSH values in diagnostic subgroups of schizophrenia



Bar diagram showing the prevalence of subclinical hypothyroidism in diagnostic subgroups of schizophrenia



The above bar diagram shows the prevalence of subclinical hypothyroidism in diagnostic subgroups of schizophrenia. 28.6% of the paranoid schizophrenia subgroup and 15.0% of the undifferentiated schizophrenia subgroup had subclinical hypothyroidism.

Table 25: Chi-Square test to compare proportions

TYPE OF SCHIZOPHRENIA	Subclinical hypothyroidism					
	Yes		No		Total	
	N	%	N	%	N	%
Paranoid	22	28.6	55	71.4	77	100.0
Hebephrenic	0	.0	3	100.0	3	100.0
Undifferentiated	3	15.0	17	85.0	20	100.0
Total	25	25.0	75	75.0	100	100.0

Chi-Square Test	Value	P-Value
Fisher's Exact Test	1.920	0.372

The above table shows that there was no significant difference between the diagnostic groups in the presence of subclinical hypothyroidism. ($p>0.05$).

DISCUSSION

The aim of the present study was to estimate the prevalence of thyroid dysfunction in patients with schizophrenia and to assess the correlation between severity of psychopathology and the levels of thyroid hormones. The study population was obtained from the out patient department of Institute of Mental Health, Chennai. The sample consisted of one hundred patients who were diagnosed to be suffering from schizophrenia as per the ICD 10 criteria. Subjects with a prior diagnosis of thyroid disorder were not included in the study. Subjects with any concurrent neurological or systemic illness which were thought to impair the thyroid function were excluded from the study. The mean age of the study sample was 33.19±6.115. The study sample consisted of 59% of females and 41% of males.

Illness characteristics of the study population was also noted. The mean age of onset of illness was 27.81±5.80. The mean duration of untreated psychosis was 28.03±27.60. The mean duration of illness in the sample was 63.59±53.52 months. The mean duration of treatment was 31.52±50.10. The mean PANSS total score obtained was 70.31±9.09.

The mean values of thyroid hormones did not show statistical difference between males and females. Hence gender differences has not contributed to the variations in thyroid hormone values ($p>0.05$).

The types of schizophrenia observed in the study population were Paranoid, Hebephrenic and Undifferentiated subgroups. The pharmacological treatments received in the sample was Haloperidol, Risperidone, and Olanzapine.

Prevalence of thyroid dysfunction in the study population

Thyroid dysfunction was assessed by considering the values of the thyroid hormones in the serum, lying outside the normal range. There was no abnormal values obtained for Free T3. 3% of the Free T4 values were in the higher than normal range. 27% of the sample had abnormal TSH values and could be categorized under subclinical hypothyroidism. This is similar to the results of the study done by R Radhakrishnan et al where they reported an abnormal thyroid hormonal status in 29% of the study population, which was comparable to that in mood disorders[53].

This showed that thyroid dysfunction existed in individuals with schizophrenia also. There was no hyperthyroidism or primary hypothyroidism reported in the study. This was in contrary to the above quoted study where the authors have shown that hypothyroidism existed in 25.17% and hyperthyroidism in 4.08% of their study sample. This could be probably due to the small sample of the present study. Probably a larger sample size could have thrown light into the disorders clearly.

A similar study conducted by Sim K et al also reported a higher percentage of thyroid dysfunction in schizophrenia of 36.4%[46]. This study was done in a sample of chronic schizophrenia patients and the authors have gone a step further by conducting the clinical assessment for thyroid function and found out only one subject had evidence of thyroid disorder clinically[46]. The sample size was larger and the subjects were chronic in patients with schizophrenia, which could have contributed to the differences obtained from the present study. The present study had not evaluated clinical thyroid status and hence it was difficult to comment whether the subjects were clinically euthyroid.

Correlation between psychopathology and thyroid hormone levels

A significant correlation was obtained between the PANSS total score and Free T4 levels in this study. The severity of psychopathology increased with increase in the Free T4 levels. These results were similar to a study conducted by A Baumgartner et al where they showed that the higher the T4 values are, the severe was the psychopathology[45]. The authors in the above study had conducted assessments in acutely ill schizophrenia patients and had found out that with neuroleptic therapy, the thyroxine levels had fallen and this was associated with a positive response to treatment[45]. Another study by Roca RP et al also found out similar results[43].

A significant association was also obtained between the positive, negative and general psychopathology scores and the Free T4 values. Data on the association between each of these scores and thyroid hormone measures were lacking in literature review.

However yet another study conducted by Jose J et al concluded that thyroid hormones were not related to the disease severity scores[49]. This could be due to the small number of cases included in that study.

A significant correlation was observed between the positive symptom of excitement and free T4 values ($p<0.05$). The negative symptoms of blunted affect, emotional withdrawal, social withdrawal, lack of spontaneity of conversation, and stereotyped thinking were significantly correlated with Free T4 values ($p<0.05$). Similarly the general psychopathology symptoms of somatic concern, anxiety, guilt feelings, depression, unusual thought content, poor attention, disturbance of volition, pre occupation and active social avoidance were also correlated significantly with Free T4 values ($p<0.05$). Data on these individual items and correlation with thyroxine was not available on literature review.

Even though the total PANSS score lacked a significant association with Free T3 and TSH values, on assessing the individual items, a significant correlation could be observed between the general

psychopathology symptoms of guilt feelings, and the Free T3 values($p<0.05$). The symptoms of motor retardation, un coperativeness, and unusual thought content had a significant correlation with the TSH values. Similar data was not found in the literature review. This was one of the initial study which had assessed the individual item scores and thyroid hormone levels.

No association between the illness characteristics and the thyroid hormone levels were found in the study. No significant gender difference was seen in the mean thyroid hormone values in the sample. The mean values of thyroid hormones amongst the various diagnostic subgroups were also not significantly different. The rates of subclinical hypothyroidism obtained in the various diagnostic subgroups did not have statistically significant difference. The study by Southwick et al also concluded with the same finding that there was no difference between T4 values amongst the multiple diagnostic subgroups in schizophrenia[42].

CONCLUSIONS

1. The prevalence of thyroid disorder is estimated to be 27% in individuals with schizophrenia and the prevalence is comparable to that in mood disorders.

2. A significant correlation exists between the Free T4 levels and the severity of psychopathology measured using PANSS.

3. The positive, negative and general psychopathology scores were significantly correlated with Free T4 levels.

4. The thyroid hormone values in the various subgroups of schizophrenia were not significantly different.

5. The rates of subclinical hypothyroidism did not differ in the diagnostic subgroups of schizophrenia.

6. No significant correlation was found between the illness chacteristics and the thyroid hormone levels.

LIMITATIONS

1. One important limitation of the study is the small sample size taken for analysis. A larger sample may bring out the thyroid disorders much more.

2. The study is a cross sectional study. The study design limits the evaluation of a cause effect relationship between thyroid hormone levels and schizophrenia.

3. The sample was taken from a tertiary care hospital and hence may not be representative of the population of schizophrenia patients in the community.

4. The clinical assessment of thyroid status was not undertaken in this study which could help in the correct interpretation of thyroid function in the sample.

FUTURE DIRECTIONS

1. Longitudinal studies following up the thyroid hormone levels during the course of schizophrenic illness can be undertaken. This can help in the careful interpretation of thyroid hormone values and the need for treatment in cases of abnormal thyroid hormone measures.

2. Familial and perinatal measurements of thyroid hormones can be done and follow up studies carried out to understand how the changes in thyroid hormones affect the psychopathology.

3. CSF analysis for thyroid hormones can be done to get a clear understanding about the thyroid – brain homeostasis.

4. The role of thyroid hormones as a biomarker in schizophrenia has to be investigated further.

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APPENDIX

Proforma

SOCIODEMOGRAPHIC DATA SHEET

Sociodemographic profile

Name:

Age:

Sex:1.Male

2.female

Education:

1.profession or honours

2.Graduate or Post graduate

3.intermediate or post high school diploma

4.high school certificate

5.middle school certificate

6.primary school certificate

7.illiterate

Occupation:

1.profession

2.Semi- profession

3.clerical, shop –owner, farmer

4.skilled worker

5.Semi-skilled worker

6.Unskilled worker

7.Unemployed

Income:

1.>32050
2.16020- 32049
3.12020-16019
4.8010-12019

5.4810-8009
6.1601-4809
7.<1600

Marital status:

1.Married

2.Divorcee

3.Single

Socioeconomic status:

1.upper

2.upper middle

3.lower middle

4.upper lower

5.lower

Residence:

1.urban

2.semi urban

3.rural

Type of family:

1.joint

2.nuclear

Religion:

1.hindu

2.christian

3.muslim

4.others

Illness characteristics:

1.age of onset of illness (years):

2.Duration of illness (months):

3.Lag period for Treatment (months):

4.duration of treatment (months):

5.treatment received:

Types of schizophrenia:

1.Paranoid

2.Hebephrenic

3.Catatonic

4.Undifferentiated

5.Post schizophrenic depression

6.Residual

7.Simple schizophrenia

8.Other schizophrenia

9.Scizophrenia, unspecified

TREATMENT RECEIVED :

1.Haloperidol

2.Chlorpromazine

3.Risperidone

4.Olanzapine

5.Clozapine

6.Aripiprazole

7.Quetiapine

8.Amisulpride

9.Trifluoperazine

POSITIVE AND NEGATIVE SYNDROME SCALE (PANSS) RATING CRITERIA

GENERAL RATING INSTRUCTIONS

Data gathered from this assessment procedure are applied to the PANSS ratings. Each of the 30 items is accompanied by a specific definition as well as detailed anchoring criteria for all seven rating points. These seven points represent increasing levels of psychopathology, as follows:

1- absent

2- minimal

3- mild

4- moderate

5- moderate severe

6- severe

7- extreme

In assigning ratings, one first considers whether an item is at all present, as judging by its definition. If the item is absent, it is scored 1, whereas if it is present one must determine its severity by reference to the particular criteria from the anchoring points. The highest applicable rating point is always assigned, even if the patient meets criteria for lower points as well. In judging the level of severity, the rater must utilise a holistic perspective in deciding which anchoring point best characterises the patient's functioning and rate accordingly, whether or not all elements of the description are observed.

The rating points of 2 to 7 correspond to incremental levels of symptom severity:

- A rating of 2 (minimal) denotes questionable or subtle or suspected pathology, or it also may allude to the extreme end of the normal range.
- A rating of 3 (mild) is indicative of a symptom whose presence is clearly established but not pronounced and interferes little in day-to-day functioning.
- A rating of 4 (moderate) characterises a symptom which, though representing a serious problem, either occurs only occasionally or intrudes on daily life only to a moderate extent.
- A rating of 5 (moderate severe) indicates marked manifestations that distinctly impact on one's functioning but are not all-consuming and usually can be contained at will.
- A rating of 6 (severe) represents gross pathology that is present very frequently, proves highly disruptive to one's life, and often calls for direct supervision.
- A rating of 7 (extreme) refers to the most serious level of psychopathology, whereby the manifestations drastically interfere in most or all major life functions, typically necessitating close supervision and assistance in many areas.

Each item is rated in consultation with the definitions and criteria provided in this manual. The ratings are rendered on the PANSS rating form overleaf by encircling the appropriate number following each dimension.

PANSS RATING FORM

		absent	minimal	mild	moderate	moderate severe	severe	extreme
P1	Delusions	1	2	3	4	5	6	7
P2	Conceptual disorganisation	1	2	3	4	5	6	7
P3	Hallucinatory behaviour	1	2	3	4	5	6	7
P4	Excitement	1	2	3	4	5	6	7
P5	Grandiosity	1	2	3	4	5	6	7
P6	Suspiciousness/persecution	1	2	3	4	5	6	7
P7	Hostility	1	2	3	4	5	6	7
N1	Blunted affect	1	2	3	4	5	6	7
N2	Emotional withdrawal	1	2	3	4	5	6	7
N3	Poor rapport	1	2	3	4	5	6	7
N4	Passive/apathetic social withdrawal	1	2	3	4	5	6	7
N5	Difficulty in abstract thinking	1	2	3	4	5	6	7
N6	Lack of spontaneity & flow of conversation	1	2	3	4	5	6	7
N7	Stereotyped thinking	1	2	3	4	5	6	7
G1	Somatic concern	1	2	3	4	5	6	7
G2	Anxiety	1	2	3	4	5	6	7
G3	Guilt feelings	1	2	3	4	5	6	7
G4	Tension	1	2	3	4	5	6	7
G5	Mannerisms & posturing	1	2	3	4	5	6	7
G6	Depression	1	2	3	4	5	6	7
G7	Motor retardation	1	2	3	4	5	6	7
G8	Uncooperativeness	1	2	3	4	5	6	7
G9	Unusual thought content	1	2	3	4	5	6	7
G10	Disorientation	1	2	3	4	5	6	7
G11	Poor attention	1	2	3	4	5	6	7
G12	Lack of judgement & insight	1	2	3	4	5	6	7
G13	Disturbance of volition	1	2	3	4	5	6	7
G14	Poor impulse control	1	2	3	4	5	6	7
G15	Preoccupation	1	2	3	4	5	6	7
G16	Active social avoidance	1	2	3	4	5	6	7

INFORMED CONSENT FORM

Title of the study:"_A study to estimate the prevalence of thyroid dysfunction and to assess the correlation between thyroid hormone levels and the severity of psychopathology in patients with schizophrenia_____".

Name of the Participant: _____.

Name of the Principal Investigator: Dr.Parvathy J Ravikumar_____.

Name of the Institution: Instituite of mental health Chennai
_____.

Name and address of the sponsor / agency (ies) (if any):__No_____
_____.

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "**__A study to estimate the prevalence of thyroid dysfunction and to assess the correlation between thyroid hormone levels and the severity of psychopathology in patients with schizophrenia**.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.*****
7. I have not participated in any research study within the past _____month(s). *****
8. I have not donated blood within the past _____ months—Add if the study involves extensive blood sampling. *****
9. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital. *****
10. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent. *****

11. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
12. I have understand that my identity will be kept confidential if my data are publicly presented
13. I have had my questions answered to my satisfaction.
14. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature / thumb impression of the participant (or legal representative if participant incompetent)

Name _____ Signature_____ Date_____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature_____ Date_____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____ Date_____

Name and Signature of the investigator or his representative obtaining consent :

Name _____ Signature_____ Date_____

Name and Signature of the guardian of the participants consent :

Name _____ Signature_____ Date_____

INFORMATION SHEET

Title of the study:"_A study to estimate the prevalence of thyroid dysfunction and to assess the correlation between thyroid hormone levels and the severity of psychopathology in patients with schizophrenia _____

_____".

Name of the Participant:
_____.

Name of the Principal Investigator: Dr.Parvathy J Ravikumar_____.

Name of the Institution: Institiute of mental health Chennai
_____.

• You are selected for this study
• We are conducting a study on thyroid dysfunction among schizophrenia patients attending Institute
Of mental Health, Madras Medical College, out patient department, Chennai
and for that your blood specimen may be valuable to us.

• The purpose of this study is to diagnose the prevalence of thyroid dysfunction in schizophrenia patients

- we are to inform you that this study has no effect on the condition you are suffering from in any way and no change in the treatment and this study is not going to alter your treatment at any time during the course of your study
- no drugs or psychotherapy are going to be administered to you in this study

• The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

• Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

• The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator

Signature of participant

Date :

INFORMATION TO PARTICIPANTS

Title: **A STUDY TO ESTIMATE THE PREVALANCE OF THYROID DYSFUNCTION AND TO ASSESS THE CORRELATION BETWEEN THYROID HORMONE LEVELS AND PSYCHOPATHOLOGY IN PATIENTS WITH SCHIZOPHRENIA**

Principal Investigator: Dr. Parvathy J Ravikumar

Name of Participant:

Site: Institute Of Mental Health, Chennai

You are invited to take part in this research. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of research?

Schizophrenia is a common mental disorder characterized by abnormal social behavior and failure to recognize what is real. It usually presents as false beliefs, unclear or confused thinking, auditory hallucinations, reduced social engagement and emotional expression .Schizophrenia is a major cause of disability and symptoms may continue for a lifetime. Some people may recover completely and function well in life.. We want to test the severity of the symptoms of patients with schizophrenia and to assess the thyroid hormone levels and analyse whether any relation exists between the two.

We have obtained permission from the Institutional Ethics Committee.

The study design

All patients in the study will be assessed for the severity of the symptoms based on The Positive And Negative Syndrome Scale (PANSS),which is a brief interview requiring 45 to 50 minutes to administer, and their Thyroid Hormone levels will be analysed by laboratory methods, from their blood specimen.

Study Procedures

The study involves evaluation of psychopathology and thyroid hormone levels for which we will be assessing your symptoms, and blood specimen will be taken for measuring your thyroid hormone levels . The assessment will be done during the period

of your hospital stay and you won't be asked to visit the hospital after the initial assessement, as a part of the study.

These tests are helpful to evaluate your condition, and to find out if any thyroid hormone level abnormality is there. Blood specimen will be collected in the morning hours in a 12 hour fasting state inside the hospital itself and Free T3, Free T4 and TSH levels will be measured.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, Institutional Ethics Committee and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not loose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to discontinuing form the study.

Signature of Investigator

Signature of Participant

Signature of the Guardian

Date

Date

ஆராய்ச்சி தகவல் தாள்

தலைப்பு : **மனசிதைவு நோய் பாதிப்பு உள்ளவர்களிடம் தைராய்டு செயலிழப்பு மதிப்பீடு மற்றும் மனநோயாலியுடன் தைராய்டு ஹார்மோனின் தொடர்பு பற்றி ஒரு ஆய்வு**

ஆய்வாளரின் பெயர் : **மரு. பார்வதி** J. **ரவிக்குமார்**

பங்குகொள்பவரின் பெயர் : _____

பங்குபெறும் இடம் : அரசு மனநல காப்பகம், சென்னை மருத்துவக் கல்லூரி, சென்னை

ஆராய்ச்சியின் நோக்கம்

அரசு மனநல காப்பக புறப்பிணியாளர்கள் பிரிவுக்கு வருகை தரும் 18 முதல் 40 வயதுக்குட்பட்ட மனச்சிதைவு நோயாளிகளிடம் நாங்கள் ஒரு ஆய்வு மேற்கொள்கிறோம். மனச்சிதைவு நோய்க்கும் தைராய்டு மற்றும் மனச்சிதைவு நோயாளிகளில், தைராய்டு சுரப்பி பிறழ்ச்சி விகிதத்தை அறிவதே இந்த ஆய்வின் நோக்கம்.

இந்த ஆய்வுக்காக தங்கள் இரத்த மாதிரியை சேகரித்து, அதில் தைராய்டு ஹார்மோன் அளவை பிரசோதிக்க வேண்டும்.

இதனால் தங்களுக்கு எந்தவிதமான பாதிப்புகளும் ஏற்படாது என்றும் அவரது சிகிச்சை முறையில் எந்த மாற்றமும் செய்யப்படமாட்டாது என்றும், இந்த ஆராய்ச்சிக்காக எந்த குறிப்பிட்ட மருந்துகளும் பரிசோதனைக்காக உபயோகிக்கப்படவில்லை என்றும் உறுதியளிக்கிறோம்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.ள

இந்த ஆய்வின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய முழு விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

மேற்கூறிய அனைத்தையும் நான் நன்கு புரிந்துக்கொண்டேன். இதற்க்கு என் முழு சம்மதத்தை தெரிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர் கையொப்பம் / இடது கைரேகை

நாள் :

இடம் :

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தகவல் தாள்

தலைப்பு : **மனசிதைவு நோய் பாதிப்பு உள்ளவர்களிடம் தைராய்டு செயலிழப்பு மதிப்பீடு மற்றும் மனநோயாலியுடன் தைராய்டு ஹார்மோனின் தொடர்பு பற்றி ஒரு ஆய்வு**

ஆய்வாளரின் பெயர் : **மரு. பார்வதி ஐ. ரவிக்குமார்**

பங்குகொள்பவரின் பெயர் : _____

பங்குபெறும் இடம் : அரசு மனநல காப்பகம், சென்னை மருத்துவக் கல்லூரி, சென்னை

நான் இந்த படிவத்தை முழுவதுமாக படித்தேன். என்னுடைய சந்தேகங்களை கேட்டு தெளிவிபடுத்திக்கொண்டேன். நான் 18 – 40 வயதிற்கு மேற்பட்டவர் என்பதையும் இந்த ஆய்வாளர் மேற்கொள்ளும் இந்த ஆய்விற்கு என்னை இணைத்துக்கொள்ள முழுசம்மதம் தெரிவிக்கிறேன்.

1. நான் இந்த ஒப்புதல் படிவம் மற்றும் ஆராய்ச்சி தகவல் தாள் அனைத்தையும் படித்து அறிந்துக்கொண்டேன்.

2. ஒப்புதல் படிவம் முழுவதுமாக எனக்கு விவரிக்கப்பட்டது.

3. நான் இந்த ஆய்வின் தன்மையை பற்றிய விளக்கங்களை அறிந்துக்கொண்டேன்.

4. என்னுடைய உரிமைகளையும் மற்றும் பொறுப்புகள் என்ன என்பதையும் ஆய்வாளர் மூலம் அறிந்துக்கொண்டேன்.

5. நான் தற்பொழுது எடுத்துக்கொள்ளும் மற்றும் முன்பு எடுத்துக்கொண்ட எல்லா சிகிச்சை முறைகளையும் (இதற மருந்துவ சிகிச்சைகள் உட்பட) ஆய்வாளருக்கு தெரியபடுத்தினேன்

6. இந்த ஆய்வில் நாள் பங்குபெறுவதின் மூலம் ஏற்படும் விளைவுகளையும் நான் அறிந்துக்கொண்டேன்.

7. நான் இதற்கு முன்பு கடந்த _____ மாதங்களில் எந்தவித ஆய்வுகளிலும் பங்குபெறவில்லை.

8. நான் எந்த நேரத்திலும் இந்த ஆய்வில் இருந்து வெளியேரலாம் என்றும் இதனால் பிற்காலத்தில் எனக்கு மருத்துமனையில் கொடுக்கப்படும் சிகிச்சையில் எந்த பாதிப்பும் இருக்காது என்பதை அறிந்துள்ளேன்.

9. மேலும், எந்த நேரத்திலும், ஏதேனும் காரணத்திற்காவது ஆய்வாளர் இந்த ஆய்விலிருந்து என்னை விலக்கிவிடுவார் என்பதையும் அறிந்துள்ளேன்.

10. என்னிடம் இந்த ஆய்வின் மூலம் பெறப்பட்ட தகவல்களை ஆய்வாளர், உயர் அதிகாரிகளிடமும் அரசு இயந்தரங்களிலும் மற்றும் நெறிமுறை குழுவிற்கும் தெரியபடுத்த சம்மதிக்கிறேன். அவர்கள் என்னுடைய முழு தகவல்களை ஆராய நேரலாம் என்று அறிந்துக்கொண்டேன்.

11. என்னுடைய தகவல்களை வெளியிடும்பொழுது, என்னுடைய அடையாளங்கள் இரகசியமாக பாதுகாக்கப்படும் என்று புரிந்துகொண்டேன்.

12. என்னுடைய எல்லா கேள்விகளுக்கும் திருப்திகரமான பதில்கள் கிடைத்தன.

13. நான் தானாகவே முன்வந்து இந்த ஆய்வில் என்னை ஒரு உறுப்பினராக இணைத்துக்கொண்டேன்.

இந்த ஆய்வில், எனக்கு ஏதேனும் கேள்விகள் எழுந்தால் அதை ஆய்வாளரிடம் கேட்டு அறிந்துக்கொள்ள வேண்டும் என்பதையும் தெரிந்துக்கொண்டேன். இந்த படிவத்தில் கையெழுத்து இடுவதன் மூலம் இந்த ஆய்வின் எல்லா கருத்துக்களையும் நான் படித்து அறிந்துக்கொண்டேன் என்பதையும் தெரிவித்துக்கொள்கிறேன். இந்த படிவத்தின் நகலையும் நான் பெற்றுக்கொண்டேன்.

பங்குபெறுபவரின் பெயர் மற்றும் கையொப்பம் அல்லது கைரேகை

பெயர்_____ கையொப்பம்_____

தேதி_____

நடுநிலை சாட்சியாளரின் பெயர் மற்றும் கையொப்பம்

பெயர்_____ கையொப்பம்_____

தேதி_____

முகவரி_____ தொலைபேசி எண்_____

ஆய்வாளரின் பெயர் மற்றும் கையொப்பம்

பெயர்_____ ள்கையொப்பம்_____

தேதி_____

ஆராய்ச்சி தகவல் தாள்

தலைப்பு : **மனசிதைவு நோய் பாதிப்பு உள்ளவர்களிடம் தைராய்டு செயலிழப்பு மதிப்பீடு மற்றும் மனநோயாலியுடன் தைராய்டு ஹார்மோனின் தொடர்பு பற்றி ஒரு ஆய்வு**

ஆய்வாளரின் பெயர் : **மரு. பார்வதி ஜ. ரவிக்குமார்**

பங்குகொள்பவரின் பெயர் : _____

பங்குபெறும் இடம் : அரசு மனநல காப்பகம், சென்னை மருத்துவக் கல்லூரி, சென்னை

ஆராய்ச்சியின் நோக்கம்

அரசு மனநல காப்பக புறப்பிணியாளர்கள் பிரிவுக்கு வருகை தரும் 18 முதல் 40 வயதுக்குட்பட்ட மனச்சிதைவு நோயாளிகளிடம் நாங்கள் ஒரு ஆய்வு மேற்கொள்கிறோம். மனச்சிதைவு நோய்க்கும் தைராய்டு மற்றும் மனச்சிதைவு நோயாளிகளில், தைராய்டு சுரப்பி பிறழ்ச்சி விகிதத்தை அறிவதே இந்த ஆய்வின் நோக்கம்.

இந்த ஆய்வுக்காக தங்கள் இரத்த மாதிரியை சேகரித்து, அதில் தைராய்டு ஹார்மோன் அளவை பிரசோதிக்க வேண்டும்.

இதனால் தங்களுக்கு எந்தவிதமான பாதிப்புகளும் ஏற்படாது என்றும் அவரது சிகிச்சை முறையில் எந்த மாற்றமும் செய்யப்படமாட்டாது என்றும், இந்த ஆராய்ச்சிக்காக எந்த குறிப்பிட்ட மருந்துகளும் பரிசோதனைக்காக உபயோகிக்கப்படவில்லை என்றும் உறுதியளிக்கிறோம்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.ள

இந்த ஆய்வின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய முழு விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

மேற்கூறிய அனைத்தையும் நான் நன்கு புரிந்துக்கொண்டேன். இதற்க்கு என் முழு சம்மதத்தை தெரிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர் கையொப்பம் / இடது கைரேகை

நாள் :

இடம் :

SR.NO	NAME	AGE	SEX	EDUCATION IN YRS	OCCUPATION	INCOME	SES	RESIDENCE	MARITAL STATUS	RELIGION	FAMILY TYPE	TYPE OF SCHIZOPHRENIA	DURATION OF ILLNESS (MONTHS)	AGE AT ONSET(YRS)	DUP(MONTHS)	DOT(MONTHS)	PANSS POSITIVE	PANSS NEGATIVE	PANSS GEN PSY	PANSS TOTAL	FREE T3(pg/ml)	FREE T4 (ng/dl)	TSH (mlu/ml)	TREATMENT RECEIVED	DOSE [mg]
1	DHANALAKSHI	28	2	3	7	7	5	2	1	1	2	1	18	26	3	6	23	10	29	62	2.34	0.89	1.63	4	15
2	DEEPA	24	2	4	5	5	3	1	3	1	2	2	30	21	30	0-Jan	14	12	27	53	2.1	0.86	2.1	0	0
3	SUGANTHI	23	2	4	5	6	3	2	3	1	2	1	6	22	6	0	24	29	37	90	2.25	1.8	7.768	0	0
4	MAARI	25	2	6	7	6	5	2	3	1	2	4	60	20	1	59	19	10	19	48	3	0.86	3.3	3	8
5	MADESH	35	2	3	4	4	3	3	1	1	2	1	24	33	24	0	23	17	18	58	3	1.25	3.35	0	0
6	PAWNAMBAL	40	2	7	7	6	5	3	1	1	2	1	24	38	24	0	19	8	20	47	2.2	1.12	2.95	0	0
7	NAGAJOTHI	35	2	4	7	6	4	2	1	1	2	1	120	25	120	0	24	20	20	64	2	1.24	3.456	0	0
8	SHOBHA	40	2	6	7	7	4	1	1	1	2	1	120	30	1	119	16	16	27	59	2.2	1.34	3.367	1	20
9	CHARLES	40	1	4	5	4	4	1	1	2	2	1	24	38	24	0	29	17	26	72	2.12	1.86	4.78	0	0
10	KUMAR	30	1	6	6	6	4	3	1	1	2	1	36	27	24	12	20	19	25	64	2	1.07	3.356	3	8
11	SUBRAMANI	40	1	4	6	7	5	2	1	1	1	4	180	25	180	0	17	30	40	87	2.1	1.34	6.69	0	0
12	VELUMURGAN	34	1	6	7	7	5	1	2	1	2	1	12	33	12	0	21	9	16	46	3.1	0.86	2.256	0	0
13	KALYANAKUM	40	1	5	6	5	4	3	1	1	1	1	216	22	0	216	32	16	40	88	2.96	1.5	7.56	1	30
14	RANGAN	34	1	7	7	6	5	1	3	1	2	1	180	19	24	156	12	24	19	55	2.36	1.2	3.452	1	30
15	KARUNAMOO	34	1	6	5	4	3	3	1	1	2	4	120	24	1	120	26	17	34	77	2.12	1.87	4.352	1	30
16	MASILLAMANI	38	1	6	5	5	4	1	3	1	1	4	120	28	120	0	24	25	41	90	2.1	1.92	4.568	0	0
17	PRABHAKARAI	21	1	7	7	6	4	3	3	1	2	4	30	18	24	6	25	28	41	94	2.35	1.88	6.63	4	20
18	CHANDRU	35	1	6	7	6	4	1	2	1	2	1	24	33	24	0	27	27	43	97	2.86	1.94	7.75	0	0
19	LAKSHMI	26	2	6	6	5	4	2	1	1	2	1	12	25	12	0	23	25	20	68	2.4	1.26	3.864	0	0
20	RANI	36	2	5	4	5	4	1	1	1	2	1	36	33	12	24	20	15	30	65	2.46	1.42	3.862	4	20
21	SITHI BANUNA	39	2	7	7	4	4	3	1	2	1	4	60	37	24	36	19	16	30	65	2.24	1.28	3.824	0	0
22	THULASI	37	2	7	7	6	5	2	1	1	1	1	180	15	60	120	18	16	28	62	2	0.89	4.082	1	30
23	JOTHI	26	2	4	7	4	4	1	3	2	2	1	60	21	2	24	21	17	27	65	2.2	1.08	7.662	3	8
24	SELVI	36	2	7	7	6	5	1	1	1	2	1	24	34	24	0	23	19	24	66	2	1.18	4.45	0	0
25	MARY EMILDA	40	2	4	7	7	4	1	3	2	2	1	180	25	1	180	21	16	24	61	2.2	1.04	4.25	1	25
26	RAHAMATHUN	27	2	4	7	4	4	3	3	2	1	1	120	17	24	48	25	16	23	64	3.2	1.16	4.38	4	20
27	MAHARANI	40	2	2	3	2	2	3	1	1	2	1	96	32	96	0	18	18	24	60	2.12	1.03	7.78	0	0
28	SUNDARAVALI	25	2	7	6	6	4	3	1	1	1	4	6	24	6	0	19	18	27	64	3.14	1.34	4.458	0	0
29	RAJALAKSHMI	40	2	3	6	7	4	1	1	1	2	1	96	32	1	60	19	20	29	68	3.24	1.68	3.836	1	30
30	JAYABHARATH	40	2	7	6	7	4	1	1	1	2	1	24	38	2	6	24	21	29	74	2.86	1.79	4.456	4	15
31	HARIKRISHNAI	39	1	3	7	6	4	1	1	1	2	4	4	38	1	0	18	18	33	69	3.01	1.65	2.256	0	0
32	PADMANABHA	38	1	3	5	6	4	2	3	1	2	1	240	18	2	180	16	19	35	70	2.12	1.24	2.068	1	30
33	VADIVEL	20	1	4	5	6	4	1	3	1	2	1	4	19.8	1	0	17	22	30	69	2.68	1.68	3.356	0	40

34	MEENA	24	2	5	7	6	4	1	3	1	2	1	36	21	4	24	18	23	29	69	2.96	1.78	3.345	4	15
35	RAMDAS	33	1	6	6	6	4	2	1	1	2	1	60	28	6	24	19	20	28	67	3.48	1.65	2.245	3	6
36	ROSEMARY	26	2	6	3	4	3	1	3	2	1	1	60	21	12	36	21	18	30	69	2.76	1.12	7.66	3	8
37	VINOTH KUMA	33	1	2	7	5	4	1	3	1	2	1	36	30	6	24	18	14	38	70	2.45	1.82	4.489	3	8
38	RAJA	25	1	3	4	5	4	3	3	1	1	1	12	24	12	0	20	17	36	73	3.18	1.79	3.3	0	0
39	SATHISH	38	1	5	5	5	4	1	1	1	2	4	108	29	24	84	24	18	32	74	2.17	1.8	3.432	1	30
40	RAJAMUNI	39	1	4	7	6	4	2	3	1	2	1	84	32	84	0	25	17	29	71	2.86	1.69	2.23	0	0
41	VASANTHAKU	38	2	4	5	7	3	1	1	1	2	1	180	23	24	156	22	17	31	70	2.35	1.76	4.456	1	30
42	PADAPADA	39	2	7	6	6	4	2	1	1	2	4	120	29	12	60	23	16	31	70	3.09	1.9	4.984	1	30
43	GOWSAR BEG	38	2	4	7	7	5	1	3	3	1	1	132	27	12	120	23	15	29	67	2.46	1.64	6.678	3	8
44	RUTHKAMALA	40	2	7	7	6	4	1	1	3	2	1	240	20	24	216	22	7	29	58	2.19	1.45	3.345	1	30
45	ARUL	24	1	4	7	6	4	1	3	1	2	1	2	22	2	0	20	19	34	73	2.35	1.78	2.234	0	0
46	SITTHAN	36	1	7	6	7	4	1	3	1	2	4	72	30	72	0	20	14	29	63	2.38	1.65	4.456	0	0
47	MANJULA	35	2	7	5	6	4	1	1	1	2	1	60	30	60	0	20	13	29	62	2.47	1.45	1.128	0	0
48	RAJKUMARI	35	2	3	7	5	4	1	1	1	2	1	12	34	12	0	19	15	29	63	2.1	1.65	2.34	0	0
49	SELVI	40	2	6	6	6	4	2	3	1	2	4	120	30	60	60	19	16	30	65	2.12	1.67	7.765	4	20
50	PADMA	40	2	6	5	6	4	1	1	1	2	1	48	36	8	40	19	17	34	70	2.14	1.76	1.254	1	25
51	PREMANAND	40	1	6	4	5	4	1	1	1	2	1	144	28	24	120	18	15	39	72	2.12	1.75	5.568	1	30
52	KOLANDAVEL	23	1	6	7	5	4	1	1	1	2	2	12	22	12	0	18	17	34	69	2.43	1.68	2.784	0	0
53	AMUTHA	36	2	3	4	4	3	3	1	1	2	1	15	35	15	0	18	20	34	72	2.45	1.78	6.642	0	0
54	ARUMUGAM	36	1	3	5	4	3	3	1	1	2	1	84	29	36	48	17	19	37	73	2.37	1.76	3.346	3	8
55	SUKUMAR	34	1	5	6	6	4	1	1	1	2	1	60	29	60	0	19	21	34	74	2.14	1.89	4.432	0	0
56	SIVAKUMAR	38	1	5	6	6	4	1	1	1	2	4	24	36	24	0	22	21	33	76	2.54	1.88	2.278	0	0
57	GOMATHI	30	2	4	6	5	4	1	3	1	2	2	96	22	24	36	23	20	33	76	3.21	1.68	2.278	3	8
58	DHANAMANI	36	2	3	5	6	3	1	1	1	2	1	120	26	36	84	21	22	31	74	2.15	1.82	3.897	1	30
59	VENNILLA	40	2	5	5	5	4	3	1	1	2	1	36	37	36	0	18	21	32	71	2.32	0.9	7.78	0	40
60	VALLIPADMAV	39	2	5	5	6	4	3	1	1	2	1	60	34	24	36	17	18	35	70	3.45	1.2	6.986	1	25
61	MEENA	34	2	5	6	5	4	1	1	1	2	1	72	28	24	36	19	19	33	71	2.13	1.32	5.2	4	20
62	PAKKIYARATH	40	2	4	5	6	4	1	1	1	1	1	60	35	60	0	20	17	36	73	2.46	1.56	3.245	0	0
63	SELVI	32	2	4	6	6	4	3	1	1	2	1	24	30	24	0	20	20	30	70	2.34	1.32	4.324	0	0
64	MAHALAKSHM	34	2	5	5	6	4	1	1	1	2	1	48	30	48	0	18	21	27	66	2.4	1.56	3.824	0	0
65	SHANTHI	30	2	4	6	5	4	1	1	1	2	4	24	28	24	0	26	20	29	75	2.96	1.87	4.324	0	0
66	ARUL	40	1	3	6	6	4	1	1	1	2	1	36	37	36	0	25	19	31	75	2.84	1.8	3.246	0	0
67	KAMESH	33	1	4	6	5	4	3	2	1	1	4	48	29	24	24	26	19	30	75	2.1	1.76	2.134	4	20
68	KANNAN	24	1	3	7	5	4	1	1	1	1	1	36	21	36	0	23	19	32	74	2.96	1.78	3.426	0	0

69	MARY	20	2	3	5	6	4	1	2	2	2	1	12	19	12	0	23	18	34	75	2.88	0.99	6.68	0	0
70	VASANTHI	24	2	2	6	5	4	1	3	1	2	1	60	19	60	0	22	21	32	75	2.32	1.89	3.246	0	0
71	SAGUNTHALA	39	2	6	6	6	4	1	1	1	2	1	72	33	36	36	23	20	30	73	3.21	1.82	3.426	1	30
72	KALA	27	2	6	6	5	4	1	1	1	2	1	20	25	20	0	21	18	32	71	2.1	0.87	6.642	0	0
73	FAIZAL	30	1	3	4	4	3	1	1	2	2	1	60	25	12	48	19	16	35	70	2.34	0.86	7.082	1	30
74	ABDUL	32	1	2	7	6	4	1	1	2	1	1	24	31	24	0	17	15	34	66	2.56	1.24	7.762	0	0
75	MUNIYAMMA	37	2	5	7	6	4	1	1	1	1	1	84	30	48	36	18	18	31	67	2.89	1.1	3.3	3	8
76	KAVITHA	33	2	4	7	6	4	1	1	2	2	1	24	31	24	0	18	18	32	68	2.67	1.23	3.21	0	0
77	FAZAL	28	1	4	3	4	3	1	2	2	2	4	12	27	12	0	18	16	29	63	2.12	0.84	2.1	0	0
78	MEENA	35	2	3	6	6	4	1	1	1	2	1	60	30	24	36	18	17	36	71	2.78	1.96	4.78	4	20
79	RAJAMANI	30	2	4	7	6	4	1	1	1	2	1	36	27	36	0	18	18	33	69	2.76	0.88	7.78	0	0
80	MOHAN	38	2	5	7	5	4	1	1	1	2	1	72	32	24	48	16	20	33	69	2.54	1.76	1.63	0	0
81	ROBERT	29	1	4	4	5	3	1	1	2	2	1	20	27	20	0	19	19	34	72	2.65	1.78	4.61	0	0
82	IRUDHAYARAJ	40	1	5	6	5	3	1	1	2	2	1	60	35	24	36	18	17	28	63	2.34	1.74	6.68	3	8
83	DAVID	34	1	5	7	6	4	1	1	2	1	4	60	29	36	24	20	19	32	71	2.98	1.77	1.16	1	25
84	KANAGA	21	2	4	6	5	4	3	1	3	2	4	36	18	36	0	20	20	35	75	2.34	1.86	3.324	0	0
85	GAYATHRI	36	2	5	7	6	4	2	1	1	1	1	48	32	24	24	19	15	34	68	2.14	1.33	2.87	4	20
86	MALAR ELDA (	28	2	2	2	5	4	2	3	2	2	1	48	24	36	12	12	28	41	81	2.34	3.24	0.248	4	20
87	KARTHICK	24	1	4	7	6	4	1	1	1	1	1	36	21	24	12	27	23	32	82	2.95	1.76	4.326	1	25
88	VIJAYA	40	2	3	4	4	3	2	1	1	2	1	48	36	48	0	28	20	32	80	2.1	1.95	3.384	0	0
89	SHEELA	38	2	4	6	5	4	2	3	3	2	1	60	33	24	36	22	19	29	70	2.32	0.86	8.356	1	25
90	KALPANA	30	2	4	7	5	4	3	1	1	2	1	72	24	12	12	24	17	34	75	2.32	0.88	7.756	4	15
91	ADIABADAM	35	1	4	6	5	5	2	1	3	2	4	48	31	48	0	20	29	34	83	2.65	3.64	1.128	0	0
92	RAMALINGAM	19	2	3	4	4	3	1	2	1	2	1	12	18	12	0	27	17	33	77	2.43	1.64	4.432	0	0
93	SELVAM	38	1	4	7	6	4	1	1	1	2	1	36	35	36	0	25	20	29	74	2.34	1.78	2.28	0	0
94	RAMWAD	35	1	4	7	5	4	1	1	1	1	1	96	27	36	60	24	18	31	73	3.21	1.64	1.146	3	8
95	MURUGAVEL	27	1	5	4	4	3	1	1	1	2	1	24	25	24	0	20	17	31	68	3.45	0.86	7.764	0	0
96	KALAISELVAN	30	1	2	3	3	3	1	1	1	2	1	36	27	12	24	19	20	30	69	2.32	0.96	6.678	4	20
97	SRIRAM	40	1	4	6	5	3	3	1	1	2	4	36	37	36	0	19	19	27	65	2.14	1.25	2.862	0	0
98	GEETHA	29	2	4	5	5	4	1	1	2	1	1	12	28	12	0	29	23	38	90	3.68	3.42	0.29	0	0
99	SADIYA BEGU	27	2	2	3	3	3	1	1	3	2	1	48	23	24	24	21	21	22	64	2.32	0.86	7.786	1	20
100	DHANAM	39	2	4	7	5	4	1	1	1	1	1	120	29	36	84	26	19	48	93	2.45	1.94	1.198	1	30

P1(DELUSIONS)	P2 (CON)	P3 (HALL)	P4 (EXCITE)	P5 Grandiosit y	P6 (suspicion)	P7 (hostility)	N1	N2	N3	N4	N5	N6	N7	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10	G11	G12	G13	G14	G15	G16
4	2	5	1	3	5	3	1	1	2	1	2	2	1	1	1	1	1	1	2	2	3	1	1	3	5	2	1	3	1
2	5	2	1	1	1	2	3	1	2	1	2	1	2	2	2	1	1	4	1	1	2	1	1	1	4	1	1	3	1
5	3	4	1	3	4	4	4	5	4	4	4	4	4	1	3	1	1	1	1	1	4	4	1	3	4	4	1	3	4
3	3	3	1	3	3	3	2	2	1	1	2	1	1	1	1	1	1	1	1	1	2	1	1	1	3	1	1	1	1
4	2	4	2	3	4	4	3	3	3	3	3	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	1	1	1
4	3	4	1	1	3	3	1	1	2	1	1	1	1	1	1	1	1	1	1	1	2	2	1	1	3	1	1	1	1
5	4	4	2	1	4	4	3	3	3	3	4	2	2	1	1	1	1	1	1	1	3	1	1	1	3	1	1	1	1
4	1	1	1	1	4	4	2	2	3	2	3	3	1	1	1	1	1	1	1	1	3	3	1	1	4	3	1	3	1
5	4	4	2	4	5	5	3	3	3	3	3	1	1	1	1	1	1	1	1	1	4	1	1	1	4	3	1	1	3
5	1	1	1	3	5	4	4	1	4	4	1	1	4	1	1	1	1	1	1	1	4	3	1	1	3	1	1	1	3
3	2	3	2	1	3	3	5	4	5	5	4	4	3	1	1	1	1	4	1	1	4	3	1	4	4	4	3	3	4
5	1	1	1	4	5	4	1	1	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6	2	2	4	6	6	6	3	3	2	2	3	2	1	1	1	1	1	4	1	1	5	4	1	4	5	4	2	3	2
4	1	1	1	1	3	1	4	3	3	3	4	3	4	1	1	1	1	1	1	1	2	1	1	1	3	1	1	1	1
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